Dissertation on

"CLINICAL PROFILE, ETIOLOGY OF ACUTE LIVER FAILURE IN CHILDREN BETWEEN 1 MONTH - 12 YRS"

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BRANCH - VII

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CERTIFICATE

This is to certify that the dissertation entitled **CLINICAL PROFILE, ETIOLOGY OF ACUTE LIVER FAILURE IN CHILDREN BETWEEN 1 MONTH - 12 YRS** submitted by **DR. A.S.VAANMATHI** 2015-2018 session at Madras Medical College to the Faculty of Paediatrics, The Tamil Nadu Dr. M.G.R Medical University, Chennai in partial fulfillment of the university rules and regulations for award of M.D., Degree in Paediatrics (BRANCH VII) is a bonafide research work carried out by her under our direct supervision and guidance.

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DECLARATION

This dissertation entitled **"CLINICAL PROFILE AND ETIOLOGY OF ACUTE LIVER FAILURE IN CHILDREN BETWEEN 1MONTH TO 12YEARS"** is a bonafide work done by **Dr A.S.VAANMATHI** at institute of child health Madras medical college Chennai during the academic year 2015-2018 under the guidance of Prof **Dr.NIRMALA MD.DM(GASTRO)** Professor of Department of Gastroenterology, Institute of Child Health, Chennai 600008. This dissertation submitted to The Tamil Nadu Dr.M.G.R. Medical University, Chennai towards partial fulfilment of the rules and regulations for the award of M.D Degree in Paediatrics, Branch (VII)

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I, **Dr. VAANMATHI.A.S**, solemnly declare that this dissertation entitled **CLINICAL PROFILE,ETIOLOGY OF ACUTE LIVER FAILURE IN CHILDREN BETWEEN 1 MONTH-12 YRS."** was done by me under the guidance and supervision of **DR.T.RAVICHANDRAN, MD., DCH.**

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CONTENTS

Introduction

INTRODUCTION

Acute liver failure is a disease whose etiology is enigmatic as in more than 50% of the cases the exact cause cannot be found. Even if the etiology is known it is not clear how exactly it causes fulminant hepatic failure and hence the pathophysiology is exclusive. As both etiology and pathophysiology are not clear we are forced to many novel and sometimes even experimental modalities of treatment. Inspite of all these, outcome could be quite dismal and the prognosis is said to be perplexing. The hall mark of this condition are an acute impairment of liver function the presence of hepatic encephalopathy and the absence of persisting liver disease. As the only definitive treatment is liver transplantation that is not freely available in our country the prognosis is very bad[1].

Review of literature

REVIEW OF LITERATURE

DEFINITION[1]:

Pediatric Acute Liver Failure Study Group (PALFSG) proposed the following criteria.

- Biochemical evidence of liver injury
- No history of known liver disease
- Coagulopathy not corrected by administration of Vitamin K
- INR>1.5 if patient has encephalopathy or >2 if the patient does not have encephalopathy.

Liver failure refers to the clinical stage resulting from hepatocyte dysfunction and necrosis. Impairment in liver function is characterized by deranged synthesis (coagulation) detoxification and consequent encephalopathy. There are a multitude of causative factors which differ between children and adults.

Regardless of antecedent cause the clinical presentation is similar mortality is between 60-80% despite adequate care.

Acute Liver Failure

This term is used for multisystem disorder in which severe impairment of liver function INR>1.5 with encephalopathy or INR >2 with or without encephalopathy occurs in association with hepatocellular necrosis in a patient with no recognized underlying chronic liver disease within 8 weeks of initial symptoms.

Acute Liver Failure

This term is used to describe patients without previous liver disease who develop a rapidly progressive liver failure within 4 weeks of onset of symptoms.

Hyperacute Liver Failure

If the features of acute liver failure are evident within one week of onset of symptoms it is termed as hyperacute liver failure.

Subacute Liver Failure

When the features of acute liver failure are gradual over four weeks to 12 weeks after and of symptoms and is associated with persistent icterus, ascites and or encephalopathy.

The survival appears to be inversely related to the duration of illness survival with hyper acute liver failure is 36%, subacute liver failure is 14%

Etiology[2]

The etiology of acute liver failure differs from that described in adults and also varies with age in the pediatric population causes also vary across geographic regions and countries. In developing countries where hepatitis A or E are endemic these will be the most common causes of fulminant hepatic failure.

1. Infections
    a) Viral Infections

        Hepato tropic viruses A-G

        Other viruses like Dengue, Epstein Barr Virus, Ebola Virus around Virus herpes virus.

    b) Bacterial infections
        a. Enteric fever
        b. E.coli septicemia
        c. Meningococaemia
        d. Weil's disease
        e. Congenital syphilis
    c) Protozoa infection
        a. Falciparum malaria

2. Metabolic causes
    - Wilsons disease
    - Galactosemia
    - Hereditary hemochromatosis
    - Hereditary fructose intolerance
    - Iron storage disease
    - Fatty and oxidation defects
3. Drugs
    - INH
    - Paracetamol
    - NSIADS
    - Valproate
    - Carbamazepine
4. Toxins
    - Aflatoxins
    - Amantia phalloides
    - Carbon tetrachloride
    - Iron
5. Congestive causes
    - Congenital, cyanotic heart disease
    - Congestive cardiac failure

- Circulatory shock
- Myocarditis
- Budd Chiari Syndrome

6. Miscellaneous

The most common cause of FHF in children is viral hepatitis. 0.1% of patients with hepatitis A and 1% with hepatitis B develop FHF. The prevalence of hepatitis A in FHF varies from 1 to 30% and that of hepatitis B from 25 to 75%.[2]

Acute Viral Hepatitis

Acute hepatitis refers to an inflammatory disorder of the liver which is usually associated with a complete clinical and histological recovery within a period of 4 to 6 weeks in children it is most commonly caused by hepatotropic viruses followed by drugs and metabolic liver disease and rarely autoimmune liver disease. Acute viral hepatitis is usually self limited mild disease which does not require any active treatment. However it may sometimes lead on to fulminant hepatitis that may require liver transplantation.

Etiology:

1. Hepatotropic Viruses

Hepatitis A – type 72 entero virus

Hepatitis B – hepadna virus

Hepatitis C – flavi virus

Hepatitis D – satellite virus

Hepatitis E – calci virus

Hepatitis G – flavi virus

Transfusion transmitted virus – DNA virus

2. Non hepatotropic viruses

Dengue

Mumps

Measles

Rubella

Echo

Coxsackie B

Epstein virus

3. Exotic Viruses

Marburg virus

Ebola virus

PATHOLOGY[3]

The basic pathology of all types of viral hepatitis is similar. There is an acute inflammation of the entire liver characterized by hepatocellular necrosis and infiltration with leucocytes and histiocytes. The necrosis is maximum in Zone III and greatest cellularity is seen in portal tracts. The sinusoids show infiltration with mononuclear cells polymorphs and eosinophils. The surviving hepatocytes stain their glycogen. Zone III hepatocytes show eosinophils change (acidophil bodies). The reticular framework is well preserved inflammatory cells disappear gradually as the patient recovers. Occasionally the patient may develop confluent or sub massive necrosis affecting substantial groups of adjacent hepatocytes usually in Zone III. If the patient develops fulminant hepatitis there is massive hepatocellular necrosis involving the whole acinus. The liver is shrunken macroscopically and the prognosis is very bad.

Hepatitis A:

It is an ancient disease described first by Hippocrates in 44BC. It is caused by type 72 enterovirus which was named hepatitis A by Mac calum in 1947. It is the most common cause of hepatitis in children. It is relatively benign disease. The incidence of fulminant hepatitis being only <0.1%.

Hepatitis B :

Hepatitis B is a partially double standard DNA virus that belongs to hepadna virus. It has a complete coding strand paired with an incomplete and noncoding strand. The virion of hepatitis B (Dane Particle) consists of surface and core. The core is formed in the hepatocyte nucleus and the surface particles in the cytoplasm. The core contains the following

- Genome of HBV which is partially double stranded DNA
- DNA Polymerase
- HBcAg
- HBeAg

The incidence of fulminant hepatitis about 1%.[4]

Hepatitis D:

It is caused by small defective RNA virus related to plant satellite virus. It is not able to replicate on its own, but is capable of infection when activated by the presence of hepatitis B virus. The interaction between two viruses is complex. Synthesis of delta virus may depress the appearance of Hepatitis B viral markers in the infected cells and may even lead to elements of active Hepatitis B viral replication. 30% of fulminant hepatitis B may be due to coincidental delta infection.

Hepatitis C:

HCV is a single stranded enveloped RNA virus. It belongs to flavi virus family. It is responsible for 90% of post transfusion hepatitis in the world and is also an important cause of sporadic non A – non B hepatitis. The incubation period is 60-90 days. It is usually a mild disease 75% being anicteric and completely asymptomatic.

Hepatitis E:

Hepatitis E is a small RNA virus non enveloped and icosahedral caused by calcivirus. Acute icteric hepatitis is the commonest type. The clinical features are similar to those of Hepatitis A. It is insidious in onset.

METABOLIC CAUSES

Wilson Disease

It is a rare autosomal recessive disease characterized by a toxic accumulation of copper in lower brain cornea, skeletal system and other tissues. It is an important cause of chronic liver disease and fulminant hepatitis in children. The abnormal gene for Wilson disease is on long arm of chromosome 13 codes for ATP7B encode copper transparently p-type ATPases. The average intake of copper in breast fed babies is 50ug/day and in older adults 1mg/day of this 50% is unabsorbed and passed in the stools and 30% is lost through the skin. The remaining 20% is absorbed within enterocytes by metallothionein which is cystein rich protein. Copper is then

exported from the enterocyte to the portal blood by the menkes protein. Absence of this protein causes accumulation of copper within the enterocytes failure of absorption and systemic copper deficiency. Acute fulminant hepatitis is characterized by progressive jaundice ascites and renal failure usually in a child or young person. Acute intravascular hemolysis may be due to destruction of erythrocytes by sudden release of copper from necrotic lymphocytes[5].

Heriditary Tyrosinaemia

The clinical presentation varies from fulminant hepatic failure to poor weight gain and renal tubular acidosis. They may also present with E.coli septicaemia and multiorgan failure. Galactosaemia, hereditary fructose intolerance type I tyrosinaemia and neonatal hemochromatosis may present as fulminant hepatic failure in neonates and infants. Disorders of fatty acid oxidation and of oxidative phosphorylation cause recurrent hepatic dysfunction and coma which may be confused with Reye syndrome.

DRUGS

These are the most important causes of fulminant hepatic failure after viral hepatitis. They are fulminant hepatic failure as a consequence of either a dose dependent toxic injury or more commonly as an idiosyncratic reaction of therapeutic doses.

Most drugs are water insoluble and hence cannot be excreted by the liver or kidney. In the liver these are converted to water soluble products so that they can be excreted easily in urine or bile. Genetic polymorphisms of proteins that biotransform and excrete xenobiotics may increase the production of potentially hepatotoxic metabolites. The mechanisms of drug induced liver injury include;

- Disrupted cell membrane
- Altered cannalicular function
- Formation of reactive intermediates
- Immune mediated injury
- Kupffer cell activation
- Stellate cell activation
- Mitochondrial dysfunction
- Endothelial injury

Synergistic injury from multiple drug exposures is emerging as a frequent cause of fulminant hepatic failure. Here single drug exposure is nontoxic but the combination compromises the ability of the liver to clear potentially toxic metabolites.

Paracetamol

Paracetamol injures the hepatocyte in a dose dependent manner. It accounts for more than 50% of cases in adults in the west. It usually occurs within 48 hours of an intentional overdose 95% of paracetamol is conjugated to sulphate and glucuronide and excreted in urine. With the ingestion of a massive dose the pathway is overwhelmed. Paracetamol is now converted to N-acetyl P-benzoquinone urine (NAPq1) by cytochrome P450 system. NAPQI is detoxified by conjugation with glutathione. With depletion of glutathione stored in the liver NAPQI binds to the cysteine groups of protein forming hepatotoxic protein adults.[5]

Paracetamol induced acute liver failure is usually due to single acute ingestions. It may also be due to chronic use of paracetamol with therapeutic intent. The concentration of paracetamol suspensions in our country varies considerably from 100mg/5ml to 250mg/5ml of a quack who does not realize this and a common cause of drug induced liver failure. One teaspoon QID of a preparation containing 250mg/5ml for one week he could develop acute liver failure.

SGPT levels will be very high exceeding 3500IU/L. In a patient with very high levels of SGPT out of proportion to jaundice paracetamol toxicity

should be considered as a cause even when historic evidence is lacking. Measurement of serum paracetamol well predicts the risk of acute liver failure only in acute over dosage. In contrast plasma levels are not reliable in chronic overdose or in the presence of other risk factors like fasting or concurrent therapy with Cyp 2E1 inducing agents. In the latter situations the diagnosis and treatment are dependent on historical and clinical laboratory findings.

Anticonvulsants:

Phenytoin, carbamazepine, valproic acid and phenobarbitone may cause acute liver failure. Liver injury occurs within 6 weeks of exposure and is almost always accompanied by severe rash and eosinophilia indicating an immune mediated injury. Phenytoin is metabolized to a highly reactive intermediate by cytochrome P450 system. Neoantigens develop if the reactive metabolic binds covalently to tissue macromolecules and antigen precipitate immune mediated injury[6].

Anti TB Drugs

Tuberculosis is quite common in our country and hence many children receive anti-TB treatment, 1% children recovery INH may develop acute hepatitis which may progress to acute liver failure.

TOXINS:

Acute liver failure could result following the ingestion of poisonous mushrooms like Amantia phalloides and Amantia verna. They contain phalloidin and amanitiatoxin which are highly hepatotoxic. The fatal dose is present in just 3 mushrooms

Ischaemic Hepatitis

This is characterized by centrilobular necrosis with preservation of the peripheral zone ,Serum AST may reach 5000 to 10000 IU/L and coagulopathy may be found in 25-50%. AST levels rapidly decrease in response to stabilization of circulation. The rapid decline in AST levels in the absence of increasing serum bilirubin or worsening coagulopathy may distinguish ischemic hepatitis from renal or toxic hepatitis. Prognosis depends upon correction of underlying cause of hepatitis.

Autoimmune Hepatitis

Autoimmune hepatitis can present as acute liver failure in children and is an example of immune dysregulation. Autoimmune hepatitis should always be ruled out as treatment with steroid may permit survival without liver transplantation. Autoimmune hepatitis occurs due to an immune reaction to liver allo antigens. With the acute presentation autoantibodies

may be absent and liver histology shows severe hepatic necrosis accompanied by interface hepatitis and plasma well infiltrates[7].

Etiology According to Age

Neonates and Infants

- Septicemia
- Inborn errors of metabolism
- Tyrosinemia
- Galactosemia
- Hereditary fructose intolerance
- Mitochondrial disorders
- Severe birth asphyxia
- Perinatal herpes simplex infection
- Hemophagocytic lymphohistiocytosis

Older children

- Viral Hepatitis A, B, B+D, E
- Parvovirus, Adenovirus
- Herpes simplex
- Hepatotoxic drugs
- Shock, ischemic hepatitis
- Hematological malignancy

- Hodgkin's lymphoma
- Leukemic infiltrates
- Autoimmune hepatitis type 2
- Wilson disease
- Inborn errors of metabolism
- Infusions
- Industrial poisons

PATHOGENESIS

Factors that are involved in fulfillment hepatic failure.

1) Injury to hepatocyte plasma membrane

The hepatocyte plasma membrane maintains the functional integrity of the cell by regulatory fluid ions and macromolecular flexes into and out of the hepatocyte. The plasma membrane may be damaged by the immune attacks of virus and drugs. This causes loss of electrolytes enzymes and coenzyme from the cells and entry of calcium into the cells causing cell death. The loss of hepatocyte is an important cause of acute liver failure[8].

2) Organelle dysfunction

The residual function of the surviving hepatocytes is determined by the damage to subcellular organelles. Calcium is responsible for the acute liver failure in metabolic diseases like Wilson disease.

- Drugs may be activated to toxic metabolites by microsomal enzyme system and there is damage to the vital macromolecules of the cells. Similarly free radicals may be produced that damage cellular lipids and proteins.

- The toxins of Amanita phalloides mushroom may affect the endoplasmic reticulum causing acute liver failure.

3) Disturbances of hepatic circulation

The hepatic circulation is compromised in acute liver failure by two features.

- Portosystemic shunting
- Impaired sinusoidal micro circulation

There features deprive the hepatocytes of adequate nutrients so that they are not able to remove circulatory toxins. This contributes to acute liver failure.

4) Regenerative capacity of liver

The final factor in the pathogenesis of acute liver failure is the regenerative capacity of the liver. If regeneration is less than degeneration acute liver failure results and it is due to the following factors.

- If the injurious process is prolonged hepatocellular regeneration is affected.
- Role of hepato trophic factors : Insulin glucagon and epidermal growth factor may help in the regeneration of hepatocytes. Hence their deficiency will aggravate degeneration[9].

Pathophysiology:

Acute liver failure is characterized by marked splanchnic and systemic arteriolar vasodilation along with hyper dynamic circulation and low arteriovenous oxygen content difference. Tissue hypoxia develops despite adequate arterial oxygen and this contributes to development of multi organ failure and is a marker of post prognosis[10].

- Microcirculatory plugging is caused by formation of micro thrombi as a consequence of activation and consumption of platelets along with the increased adhesion of leucocytes to the endothelial wall. Increased activity of CGMP results in vasodilation.

- Encephalopathy results from the accumulation of non metabolized ammonia mercaptans fatty acids and GABA. Production of false neurotransmission is enhanced due to decreased aromatic and branchial chain amino acids in the blood. The cerebral metabolism is altered. Renal failure of various degrees occurs in acute liver failure

patients. Hypovolemia caused by vasodilation microcirculatory disturbance and acute tubular necrosis are contributing factors. Rapid deterioration in the nutritional status with depletion of muscle and fat stores often occurs as a consequence of unpaired gluconeogenesis and impaired glycogen storage.

- Hypoglycemia hypophosphatemia and hypomagnesemia are common metabolic acidosis is relatively frequent due to tissue hypoxia increased peripheral lactate production and renal failure.

- Reduced hepatic synthesis of clotting factors increased consumption of clotting factors and platelets contribute to the coagulopathy associated with acute liver failure.

- Children with acute liver failure are susceptible to infections as a consequence of impaired neutrophils and Kupffer cell phagocytic function with reduced compliment levels. Induced bacterial changes in the gut flora may also contribute to this. The common infections that occur are pneumonia, urinary tract infections and spontaneous bacterial peritonitis (SPB). A vicious cycle of endotoximia circulatory collapse tissue hypoxia, increased bacterial translocation contribute to multi organ failure[11].

PATHOLOGY

Jones classification of Acute liver failure.

- Type 1 lesion
- Type 2 lesion
- Type 3 lesion

Type 1 lesion

This is the most common lesion in acute liver failure and is characterized by necrosis and loss of hepatocytes. This is seen in

- Viral hepatitis
- Toxic hepatitis
- Ischemic hepatitis
- Metabolic hepatitis (Wilson disease, neonatal hemochromatosis)

The degree and pattern of hepato cellular injury vary according to the etiology. However they do not correlate with the development of hepatic encephalopathy or cerebral edema. Besides liver biopsy is very risky on the patients. Hence establishing a pathological diagnosis is not critical in the management of the patient.

Massive confluent or multi lobular necrosis can be demonstrated at autopsy or following orthotopic liver transplantation.

Serum bilirubin varies from 10-60mg%. The damaged hepatocyte can take up and conjugate bilirubin initially but cannot excrete it into late as it is an energy dependent process thereby resulting in conjugated hyperbilirubinemia. However as the damage increases the uptake of bilirubin is also affected resulting in increase of unconjugated bilirubin also[12].

Type 2 lesion

This is characterized by the presence of microvascular fatty infiltration. The brunt of the damage is on the mitochondria and hepatocellular necrosis is insignificant. Hence jaundice is minimal and transaminases are only slightly elevated. If the patient survives the histologic recovery is complete. This picture is seen.

- Reye syndrome
- Valproate toxicity
- Acute fatty liver of pregnancy[13]

Type 3 Lesion:

This is characterized by swelling of hepatocytes and condensation of organelles and cytoplasmic elements spotty hepatocellular necrosis and macrovascular fatty infiltration are also seen. Serum bilirubin and transaminases are moderately elevated the levels being between those type 1 and type 2 lesions. This picture is seen in

- Hereditary fructose intolerance
- Type 1 tyrosinaemia

CLINICAL FEATURES

Acute liver failure affects previously healthy children with no recognized risk factors for liver disease. Children usually present with hepatitis and worsening of symptoms over a period of several days or weeks. Jaundice is the presenting symptom of most of the children and its day of onset should be noted. A prodrome of flu like illness may precede jaundice. Fever. Anorexia, vomiting, abdominal pain and fetor hepaticus are common. Altered consciousness and mental changes present later. Infants initially may present with poor feeding irritability and disturbances in sleep rhythm. Hemorrhages diathesis and ascites may develop later. A detailed history of mental changes easy bruising seizures decreased urine output contact with infections, injections, blood transfusions drug intake and family history of Wilson disease or autoimmune disease and should be excluded For neonatal and infections presenting with acute liver failure an additional history of developmental delay consanguinity prenatal or antenatal infections and neonatal death should be sought[14].

The early clinical manifestations of acute liver failure are non specific and characterized by anorexia malaise nausea and vomiting. Central nervous system manifestations include hepatic encephalopathy and cerebral edema

with raised intracranial tension. Hepatic encephalopathy is a result of inability of liver to process and excrete endogenous toxins. Raised levels of ammonia, GABA, false neurotransmitters and pro inflammatory cytokines are implicated in the pathogenesis. Identification of hepatic encephalopathy in children can be challenging as in the early stages they present with nonspecific findings such as excessive somnolence, reversal of sleep wake cycle or behavioural and personality changes[15].

Coagulopathy due to impaired production of coagulation factors results in bleeding platelet counts are affected in setting of an infection. The patient may manifest with hypoglycemia electrolyte imbalance and metabolic acidosis. Infections are common in acute liver failure as immune system is dysfunctional and invasive procedures are performed commonly. This results in gram positive gram negative and fungal infections. Infection may manifest as hypotension disseminated intravascular coagulation metabolic acidosis coronary encephalopathy oliguria and azotemia.

Acute liver failure should be suspected when a child with suspected hepatitis develops

- Persistent anorexia
- Persistent vomiting
- Deepening jaundice
- Decreasing liver span

- Relapse of initial symptoms
- Development of ascites
- Neuropsychiatric changes [16]

COMPLICATIONS

1. Hepatic encephalopathy
2. Cerebral edema
3. Coagulopathy
4. Metabolic complications
5. Electrolyte disturbances
6. Renal complications
7. Infection

1. Hepatic encephalopathy

Encephalopathy is an essential component for the diagnosis of acute liver disease. It is a consequence of hepatocellular failure directly affecting the function of the brain. The damaged liver fails to produce appropriate amounts of neuro regulatory substances and to eliminate toxins like ammonia[17].

Neuropathological changes in Hepatic encephalopathy

Grossly the brain may be normal but cerebral edema is seen in about half of the patients particularly younger patients dying with prolonged deep

coma. Microscopically the characteristic changes are seen in astrocytes rather than neurons. The astrocytes proliferate and develop prominent nuclei margination of chromatin and accumulation of glycogen. These changes are referred to as Alzheimer type 2 astrocytes These changes are found particularly in the cerebral cortex and basal ganglia and are related to hyperammonemia neurons shows minor alterations. Early astrocyte changes are probably reversible in very long standing cases the structural changes may be irreversible and the patient unresponsive to treatment. Apart from the astrocytic changes there is cortical thinning with loss of neurons in cortex basal ganglion and cerebellum demyelination in the pyramidal tract is associated with spastic paraplegia in patients with severe liver disease and minimal encephalopathy. The permeability of ammonia is increased[18].

Clinical Features:

Hepatic encephalopathy causes an organic mental reaction associated with neurological disturbance. The clinical picture depends upon the nature and intensity of the etiological and precipitating factors[19]

- Disturbed consciousness with disordered sleep
- Hypersomnia
- reversal of sleep rhythm
- Reduction of spontaneous movements
- A fixed stare

- Apathy
- Slowness and brevity of response
- Personality changes
- Irritability
- Intellectual deterioration
- Handwriting deterioration
- Constructional apraxia
- Child may micturate and defecate in inappropriate places
- Speech is slow and slurred
- Dysphasia
- Fetor hepaticus:

Sweetish slightly feculent smell of the breath which is compared to that of freshly opened corpse due to the presence of methionine derivatives lie methyl mercaptan which are usually metabolized by the liver[20].

Asterixis (Flapping tremor)

This is the most characteristic neurological abnormality. It is due to impaired inflow of joint and other afferent information to the brainstem reticular formation resulting in lapses in posture [21]

It is demonstrated with the patients arms outstretched and fingers separated or by hyper extending the wrists with the forearm fixed. There is a

rapid flexion extension movement at the metacarpophalangeal and wrist joints accompanied by lateral movement of the digits. Sometimes the neck jaw, protruded tongue, retracted mouth and highly dosed eyelids are involved and gait is ataxic. It disappears when patient becomes comatose. It is usually bilateral but asymmetric and is absent in coma. It is not specific for hepatic precoma and is also seen in renal failure, respiratory failure and congestive cardiac failure. Deep tendon reflexes are exaggerated hypertonia and ankle clonus may be seen. When comatose deep tendon reflexes are lost and flaccidity is seen. Plantar reflexes initially flexor and becomes extented in deep coma[21].

Factors that contribute to Hepatic encephalopathy

- Hypoglycemia
- Hypoxia
- Haemorrhage
- Septicemia
- Hepatotoxic drugs
- Hypokalemia
- Reduced cerebral perfusion
- Cerebral edema[22]

Clinical grading of Hepatic encephalopathy

Grade 1 : Confused altered mood or behaviour psychomotor defects no flap.

Grade 2 : Drowsy inappropriate behavior flap+

Grade 3 : Stuporous speaks and obeys simple commands

Grade 4A : Marked confusion coma responds to painful stimuli

Grade 4B : Deep coma no response to even painful stimuli

PATHOGENESIS OF HEPATIC ENCEPHALOPATHY

- Porta systemic shunting
- Alterations in the blood brain barrier
- Toxic metabolite affecting the CNS[23]

Portal systemic shunting

In hepatic encephalopathy the various toxic metabolites in the blood reach the brain directly without being detoxified by the liver. In fulminant hepatitis the shunt in through the liver itself. The damaged hepatocytes are not able to remove the toxic products in portal venous blood. Hence they pass unaltered into the hepatic veins and subsequently reach the brain. In patients with chronic liver disease like cirrhosis the portal blood bypasses the liver through large natural collaterals[24].

Ammonia is believed to play a major role in pathogens of hepatic encephalopathy by the following mechanisms.

- It combines with alpha – ketoglutarate to form glutamic acid thus removing an important link in te krebs citric acid cycle which is vital for brain metabolism.
- It has direct toxic effect on the neuronal membrane.
- It causes an indirect neuronal dysfunction due to disturbance of glutamate neurotransmission[25].

GABA and endogenous benzodiazepenes:

GABA is the principle inhibitory neurotransmitter in the brain. It is usually synthesized from glutamate by glutamate dehydrogenase in presynaptic nerves and stores and stored in vesicles. GABA binds to specific GABA receptor in the postsynaptic membrane. This receptor is part of a larger receptor complex which also has binding sites for benzodiazepines and barbiturates The binding of any of the ligand opens a chloride channel and after the influx of chloride there is hyperpolarization of the postsynaptic membrane and neuro inhibition[26].

GABA is also synthesized by gut bacteria and they entity the portal vein is metabolized by the liver. In the presence of liver failure or poor portal systemic shunting it enters the systemic circulation. There are

increased GABA levels in the plasma of patients with liver disease and hepatic encephalopathy[27].

Endogenous benzodiazepines are increased in patients with hepatic encephalopathy and these may also interact with the GABA receptor complex and cause neuro inhibition. The relationship between plasma endogenous benzodiazepines and encephalopathy is however controversial. However both central benzodiazepine receptors and peripheral type benzodiazepine receptors are increased in the brain in hepatic encephalopathy[28].

False Neurotransmitter

The following false neurotransmitter are produced in the colon by bacteria.

- Tyramine
- Octopamine
- Beta Phenylethanolamine

There reach the brain and inhibit the true transmitter likely to hepatic encephalopathy.

Role of Branched chain amino acids and aromatic amino acids

The serum level of the aromatic amino acids like tyrosine. Tryptophan and phenylalanine are increased due to poor hepatic deamination. At the same time well of branched chain aminoacids like

valine isolated and leucine are decreased due to increased metabolism by skeletal muscle and kidneys secondary to the hyperinsulinemia of chronic liver disease[29].

These two groups of amino acids compete for uptake in to the brain. As their serum level is higher, more of aromatic aminoacids pass an abnormal blood brain barrier into the brain. Phenylalanine in the brain is converted into false neurotransmitter like octopamine and phenylethanolamine which may contribute to hepatic encephalopathy.

Stages of Hepatic encephalopathy

Stage 1 (Prodrome)

- Personality changes
- Euphoria
- Child like behavior in adults infantile behavior in children
- Sleep disturbances reversal of sleep rhythm and insomnia
- Intellectual deterioration
- Inappropriate behavior bursts of anger and crying
- High pitched ear piercing screams
- Asterixis may be present

Stage 2 HE (impending coma)

- Accentuation of Stage 2
- Drowsiness
- Inappropriate behavior
- Hyperreflexia
- Incontinence
- Marked asterixis
- EEG abnormalities[30]

Stage 3 HE (Stupor)

- Depending somnolence and stupor
- Patient responds vigorous physical stimuli but goes back to sleep immediately
- Extreme agitation biting and rage

Stage 4 HE (Coma)

- 4A - Patient is comatose but responds to painful stroke
- 4B - Deep coma

2. CEREBRAL OEDEMA

This is the most common cause of death in acute liver failure. It usually occurs in stage 4 hepatic encephalopathy after a prolonged duration of coma. However at may present within 24 hours of onset of coma[31].

- Sun in 80% of fata cases
- Grade III, IV encephalopathy
- Raised head end 45’
- Fluid restriction IV mannitol
- Avoid hyperthermia
- Ventilate of hepatic encephalopathy > grade III

Pathogenesis

- Increased permeability of blood brain barrier
- Inhibition of Na- K+ ATP ase pump
- Failure of autoregulation of cerebral blood flow
- Mechanical Ventilation

It manifests as unequal or abnormality reacting pupils mild clonus or seizures and loss of brainstem reflexes. There may be alteration of respiratory bradycardia and hypertension[50].

Clinical features of cerebral edema

- Increased muscle tone in the limbs
- Trismus
- Opisthotonus
- Decerebrate posturing
- Hyperventilation
- Pupils dilated and reacting poorly light

3-COAGULOPATHY

A hemorrhage diathesis is invariable in acute liver failure as the liver plays a central role in hemostasis[32]. The following factors contribute to the

- Failure of synthesis of clotting factors and fibrinolytic factors by the damaged liver[33].
- Disturbances in the number and function of platelets
- A low grade DIC which is common on acute liver failure also contributes to coagulopathy[34].

All the clotting factors are synthesized in the liver. Hence the prothrombin time and partial thromboplastin time are prolonged[35].

Coagulopathy may be classified into

- Mild PT < 18
- Moderate PT 18-25
- Severe PT >25[36]

Thrombocytopenia is seen in 50% of patients it is caused by

- Hypersplenism
- Bone marrow suppression
- Increased consumption of platelets[37]

Common types of bleeding

- Bleeding from puncture sites
- Upper GI bleed
- Intracranial bleed[38]

4. Metabolic Complications

Hypoglycemia caused by

- Massive hepatocellular necrosis which impairs glyoneogenesis and causes glycogen depletion
- Diminished hepatic catabolism of insulin by the damaged liver.
- Increased glucose utilization due to anaerobic metabolism
- Secondary bacterial infection[39]

5. Electrolyte disturbances

Hypokalemia

This is due to inadequate replacement increased loss and secondary hyperaldosteronism. It may worsen coma and precipitate cardiac arrhythmias[40].

Hyponatremia

The total body sodium is elevated because of secondary hyperaldosteronism inhibition of Na- K+ pump also contributes.

Acid base imbalance

Respiratory alkalosis – Hyperventilation in early hepatic encephalopathy

Metabolic alkalosis – frusemide hypokalemia

Respiraory acidosis

- Respiratory failure
- Cerebral edema
- Obstructed ET tube
- Pneumonia

Metabolic acidosis

- Metabolic failure – accumulation of organic acids
- Hypotension poor perfusion lactic acidosis
- Renal failure

- Mechanical ventilation
- Citrated blood[41]

6. Renal Complications

a) Hepato renal syndrome:

The functional renal failure is the most common cause of renal failure in ALF. It is characterized by

- Normal urine sediment
- Marked sodium rectum – urine sodium <20
- Reduced urine output

b) Acute tubular necrosis:

This is due to hypotension sepsis of hemorrhage complicating ALF. It is characterized by

- Abnormal urine sediment
- Urine sodium >20mEq/L
- Severe Oliguria (outpu <0.5 l

c) Prerenal failure :

This may be due to dehydration or GI bleeding[42]

7. Infection

Septicemia is common and is due to

- Neutropenia
- Impaired cell mediated and humoral immunity
- Defective opsonization[43]
- Impaired kupffer cell function
- Frequent venipuncture and catheters[44]

INVESTIGATIONS

Infections : IgM anti HAV

IgM anti HEV

Hepatitis B surface antigen

IgM anti Hepatitis B core antigen

CMV – PCR (CMV)

IgM VZV (Varicella zoster virus)

IgM Viral Capsid Antigen (EBV[45]

Metabolic

Wilson disease	-	Cereoplasmin Kayser fluscher ring
		24 hours urinary copper
Autoimmune hepatitis	-	Anti liver kidney microsomal antibody
		Antinuclear antibody

		Anti smooth muscle antibody[46]
		Immunoglobulin levels
Tyrosenemia	-	Urinary sucinylactone levels
Galacosemia	-	Urine nonglycose reducing substances
		Galactose 1 phosphate uridyl transferase
Miscellaeous		
Hemophagocytosis	-	Triglyceride, ferritin, fibrinogen and
		Bone marrow biopsy
Paracetamol poisoning	-	Plasma levels of paracetamol

Platelet count is reduced due to consumption or reduced production. WBC count may be very high due to stress response or associated bacterial infection or low due to aplastic anemia[47].

ALT and AST are very high or their levels have fallen suddenly since their last measurement.

- Prothrombin time is very much prolonged
- Serum bilirubin may be very high
- Blood ammonia is elevated 28 hours above normal
- Blood urea nitrogen is high due to renal dysfunction increased production of urea secondary to LI bleeding and dehydration. Some

times blood urea may be low due to decreased production by Krebs urea cycle in the liver.

- Arterial blood gas analysis shows a wide spectrum of abnormalities from respiratory alkalosis to mixed respiratory and metabolic acidosis[48].

MANAGEMENT

The management of liver failure in children is based on;

i) Diagnosis of etiology as it influences the prognosis and management.

ii) Assessment of severity of liver failure and timely liver transplantation if indicated[49].

iii) Anticipation prevention and treatment of complications.

General Measures

- All secretions of the patient should be treated potentially infected capable of transmitting hepatitis.
- Sedatives should be awarded as far as possible
- Venous access is essential
- Urinary bladder should be catheterised and fluid intake and output chart maintained[50].

Management of coagulopathy

- Vitamin K 0.2-0.3mg/kg max 10mg
- Mild coagulopathy – No treatment
- Moderate : FFP 10ml/1g 6 hourly to reduce PT 16-18 seconds
- Severe : FFP 15-20ml/1g 6 hourly to reduce PT to 18-25
- Cryoprecipitate platelet transfusion[51]
- Ranitidine 1-2mg/kg/dose IV 2-4 times / day
- Omeprazole 0.5 mg/kg/dose NG 1-2 times / day
- Sucralfate 10-20mg/kg/dose NG 4-6 hourly
- Administration of recombinant factors VIIa produces temporary correction of coagulopathy.
- Sodium should be restricted to 1mEq/kg/day
- Hypokalemia should be avoided by giving 3-6mEq/kg/day
- Anemia should be corrected and Hemoglobin maintained around 12gms[52].

Treatment of cerebral edema

- Cerebral edema should be treated with 20% mannitol 1g/kg every 2-6 hours.
- Fluid restriction less than 75% maintenance
- Serum osmolality should be maintained below 320 on osm/L

- Elective ventilation should be done of cerebral edema suspected [53]
- Steroids should not be used.
- Convulsion should be controlled with phenytoin or phenobarbitione
- Cerebral perfusion pressure should be maintained by administration of blood products albumin and ionotropic agents
- Persistent convulsions indicated a grave prognosis[54].

Fluid Balance

- Intake output chart should be maintained
- The ideal maintenance fluid is 10% dextrose in 0.25% saline
- Fluid intake should be <75% maintenance[55].

Sodium

- Total intake should be restricted to 1mEq/kg/day

Potassium

Potassium requirements are quite high 3-6mEq/kg/day[56]

Management of Renal Failure

- The circulating volume should be maintained to prevent prerenal failure.
- The urine output should be >0.5m/kg/hr

- If the CVP is high frusemide . may be given in the dose of 1-2mg/kg/iv
- Renal failure usually become normal after a successful liver transplantation[57].

Hypoglycemia

Blood glucose should be monitored every 2-4 hourly 10-50% glucose IV will help to prevent e complication[58].

Cardiovascular complications

Hypotension is common due to reduced peripheral vascular resistance arteriovenous shunting. It may be refractory to volume replacement and pressure agents[59].

Secondary infections

Septicemia is seen in 50% of children with acute liver failure. It is usually caused by gram positive bacteria like staphylococcus aureus and streptococci. Gram negative bacteria and fungi may also be responsible[60].

Broad spectrum antibiotics should be started at the earliest suspicion of sepsis.

- Tachycardia
- Hypotension
- Oliguria

- Hypoglycemia
- Hypothermia
- Deterioration in mental state

Amoxicillin 75mg/kg/day in 3 doses; cefuroxime 60mg/kg/day in 3 doses in metronidazole of there is suspicion of anaerobic infusion prophylactic antifungals may also be given[61].

Specific therapy for acute liver failure

Paracetamol ingestion

N.acetyl cysteine should be started within 24 hours of ingestion and continued until liver failure has resolved[62].

Fulminant hepatitis B

In these patients lamivudine telbivudine or entecavir is indicated.

Amanita phalloides poisoning

Massive dose of benzylpenicillin may decrease the uptake of amatoxin thiotic acid (300mg/kg/day) IG infection may reduce hepatic damage[63].

The following drugs and procedures have been tried to support the liver while awaiting regeneration or transplantation

- Prostaglandin E
- Glucagon
- L-Dopamine
- Benzodiazepine receptor antagonists like flumazenil
- Exchange transfusion
- Plasmapheresis[64]
- MARS

MARS or Molecular absorbent reticulating system is cell free non biological artificial liver support system removes albumin bound toxins from the blood[65].

Extracorporeal Bio artificial liver support devices

Extracorporeal systems that combine hepatocytes in a plastic cartridge and simplex mobile membrane[66]

Liver transplantation

It is the only definitive treatment of acute liver failure, O'Grady's criteria for liver transplantation[67]

A. Paracetamol induced ALF

pH <7.3

PT >100 seconds

Serum creatinine >300 mmol/L

B. Non Paracetamol induced ALF

PT >100 seconds

or

Any three

- PT >50 seconds
- Age <10 years
- Serum bilirubin >17.5mg%
- Etiology NANB hepatitis idiopathic drug reactions
- Duration of jaundice 7 days before the onset of hepatic encephalopathy[68]

It is indicated in all children

- Stage 3 or 4 HE
- Viral hepatitis

- Paracetamol overdue
- Halothane hepatitis
- Wilson disease
- Type I tyroienemia[69]

PROGNOSIS

Prognosis is good in the following;

Age : Children >10 years

Hepatitis A

Paracetamol poisoning if treated in time

Presence of an obvious etiology

Stage of Hepatic encephalopathy in 1 and 2

Increased serum alpha fetoprotein[69]

Causes of Death

- Cerebral edema
- Overwhelming bacterial or fungal infection
- Respiratory failure
- Hemorrhagic diathesis
- Complication of liver transplantation[69]

Aims and objectives

AIMS & OBJECTIVE

The aim of my study is to study and determine the clinical profile, etiology of acute liver failure in children between 1mon-12yrs of age in tertiary pediatric centre in south india

Materials and methods

METHODOLOGY

(MATERIALS & METHODS)

STUDY DESIGN:

Prospective study

STUDY POPULATION:

Children in study age group attending gastroenterology department and admitted in medical ward satisfying the inclusion criteria.

PLACE OF STUDY:

Department of Gastroenterology and Paediatric medical ward in ICH

STUDY PERIOD :

October2016 to june 2017

SAMPLE SIZE : 50

INCLUSION CRITERIA:

All children aged 1 month to 12years presenting with acute liver failure attending the hospital

EXCLUSION CRITERIA:

Children with pre-existing liver disease

PROCEDURE

After obtaining informed consent from parent/guardian, various Patient demographic characteristics, history ,clinical details will be entered in a prestructured profoma. All these children will have basic investigations like LFT Serum albumin total proteins liver enzymes viral markers, coagulation profile.

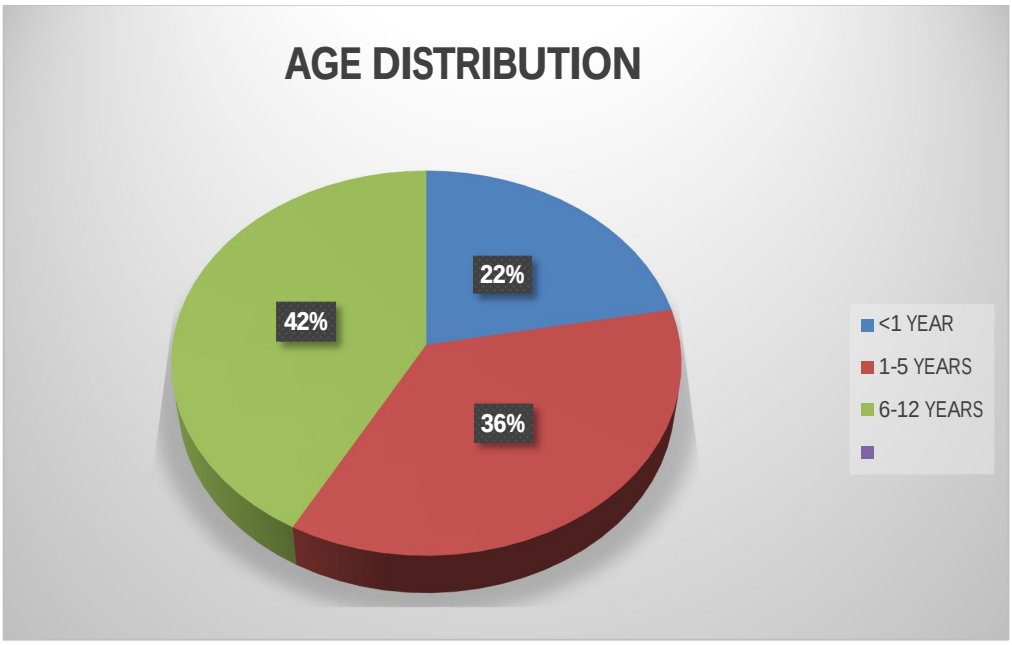
STATISTICAL ANALYSIS:

Statistical analysis of data will be performed by statistical software SPSS. Outcome variables will be categorized as normal or abnormal and their prevalence will be expressed as percentage and p value of <0.05 will be considered significant.

Results

OBSERVATION & RESULTS

Age group	<1 year	11(22%)
	1-5 years	18(36%)
	6-12 years	21(42%)

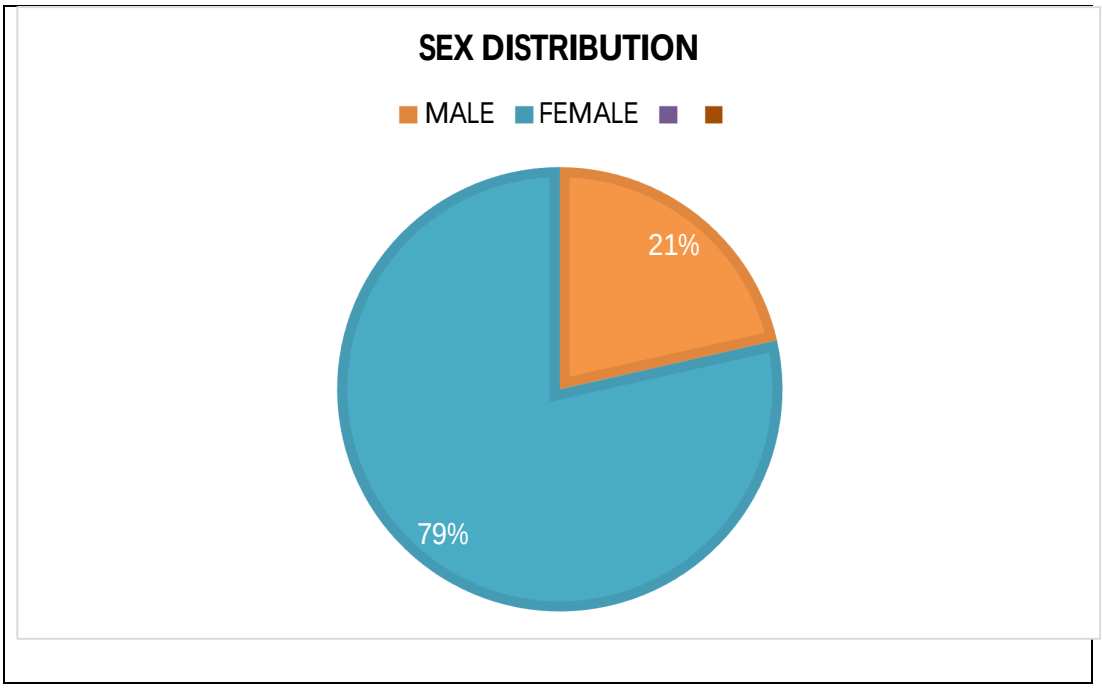


In this study, 42% of the children belong to 6-12 years, 36% belong to 1-5 years and 22% belong to <1 year group.

SEX DISTRIBUTION

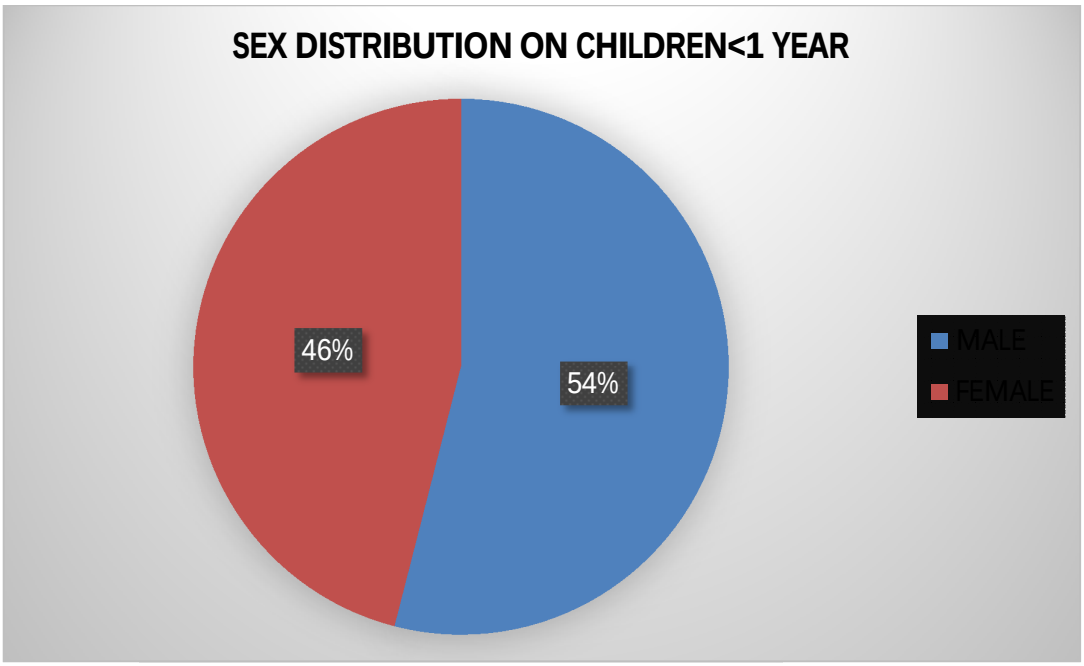
In this study, 30(60%) of the children are females and 20(40%) are males.

SEX	NUMBER
Male	20(40%)
Female	30(60%)



SEX DISTRIBUTION IN CHILDREN <1 YEAR

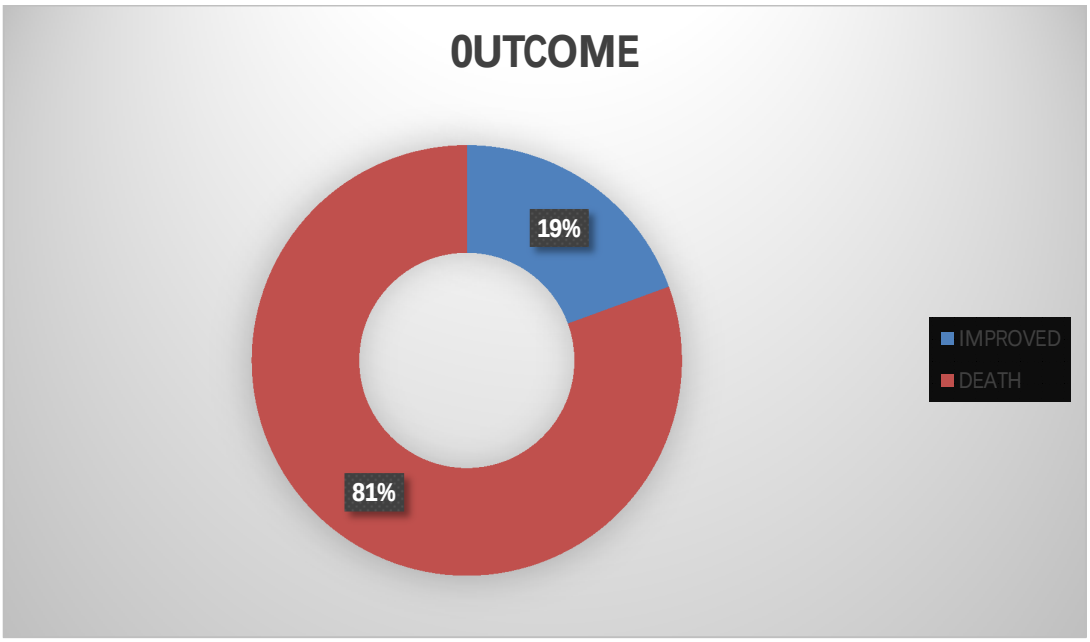
SEX	NUMBER
MALE	6(54%)
FEMALE	5(46%)



OUTCOME

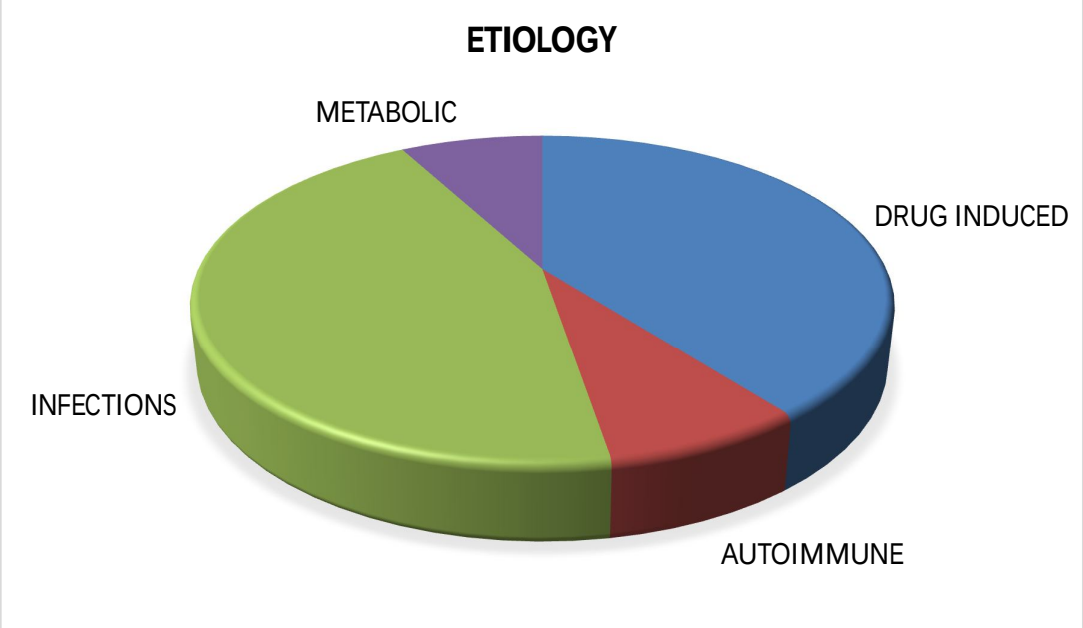
In this study, out of the 50 children studied, 16(32%) improved and 34(68%) died.

OUTCOME	NUMBER
Improved	16(32%)
Death	34(68%)



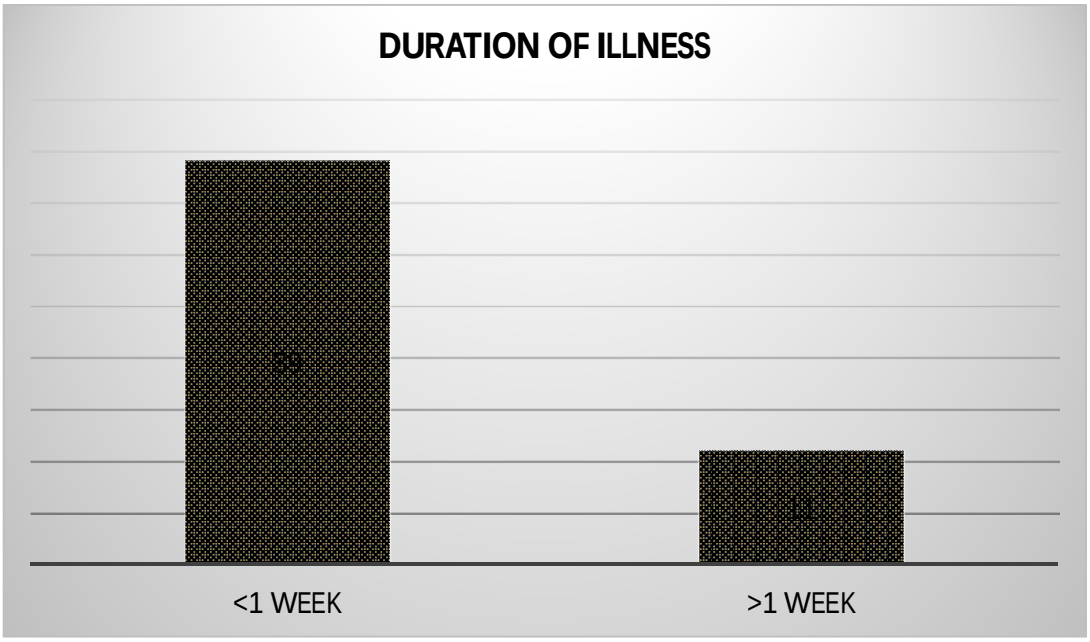
Drug induced	15(30%)
Autoimmune	3(6%)
Infection	17(34%)
Metabolic	3(6%)
Congestive	4(8%)
Inconclusive	8(16%)

In this study, the etiology of liver failiure was found to be infection(34%), drug induced(30%), inconclusive(16%), congestive causes(8%)



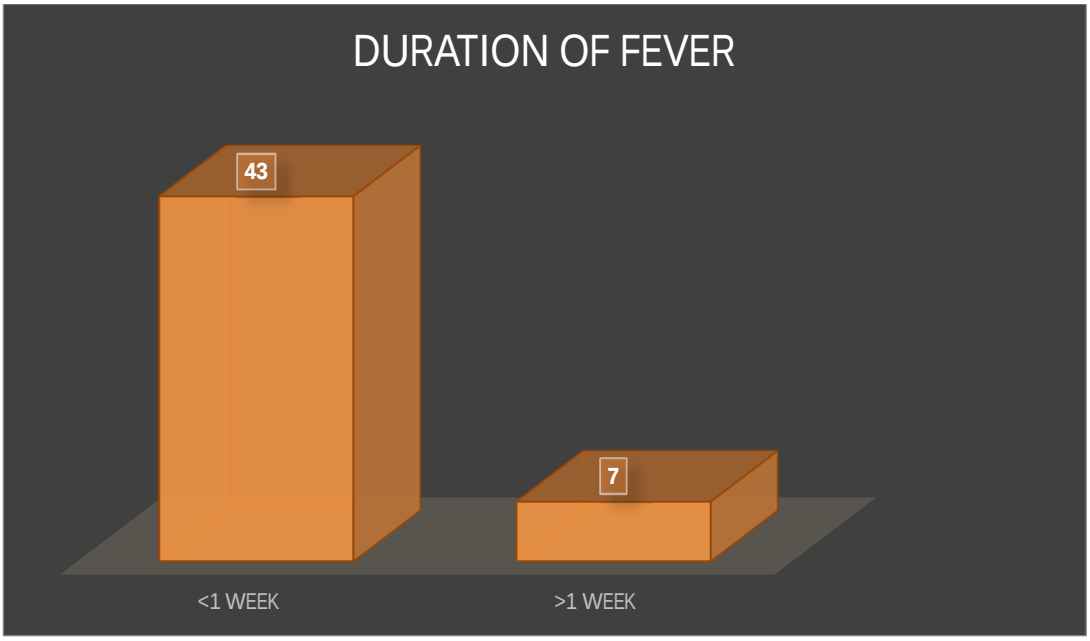
DURATION OF ILLNESS	NUMBER
<1 week	39(78%)
>1 week	11(22%)

In this study the duration of illness was found to be <1 week in (78%) and >1 week in (22%)



DURATION OF FEVER	NUMBER
<1 week	43(86%)
>1 week	7(14%)

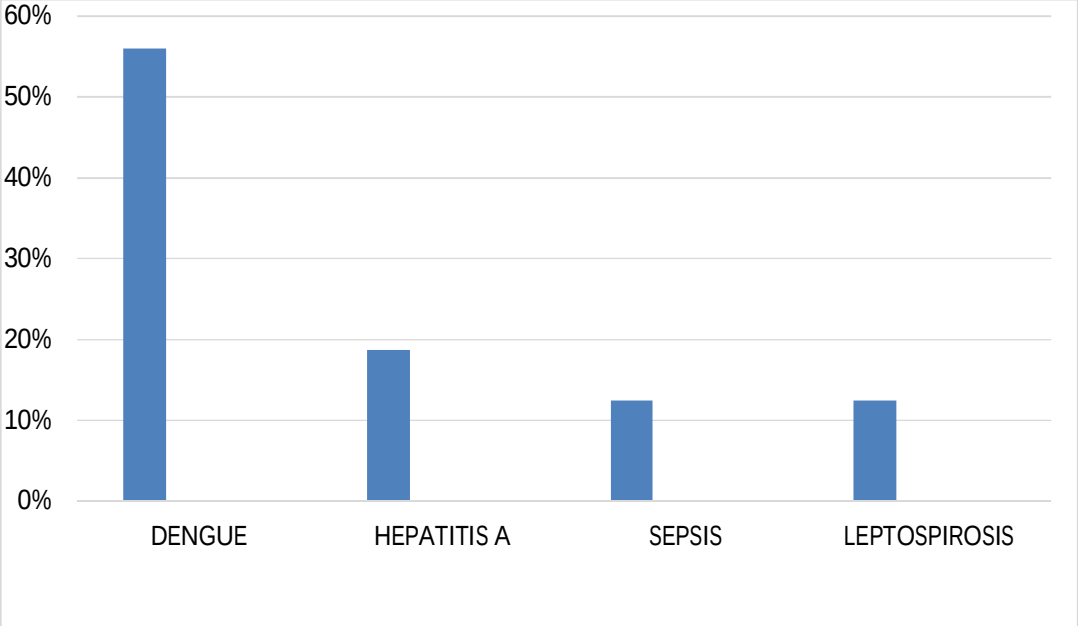
In this study, 43(86%) children had fever < 1 week duration and 7(14%) had fever >1 week duration.



ETIOLOGY AMONG INFECTIOUS CAUSES

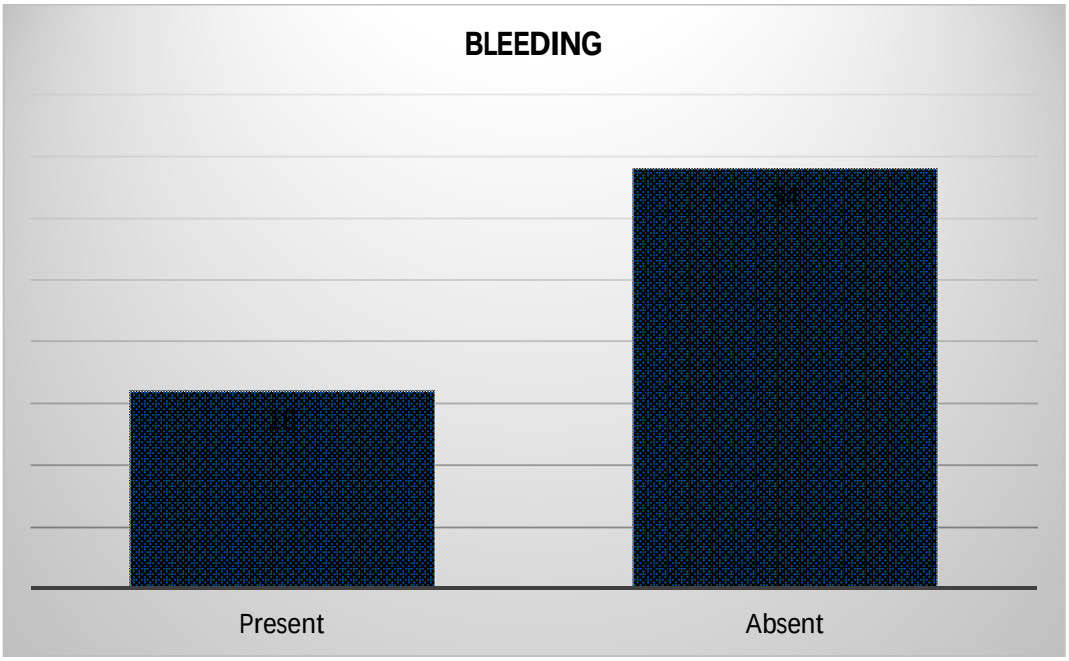
INFECTIOUS ETIOLOGY	NUMBER
DENGUE	9(56%)
HEPATITIS A	3(18.75%)
LEPTOSPIROSIS	2(12.5%)
SEPSIS	2(12.5%)

In this study among the infectious causes dengue contributed maximum of 56% while hepatitis A(18.75%) leptospirosis(12.5%) and sepsis(12.5%)



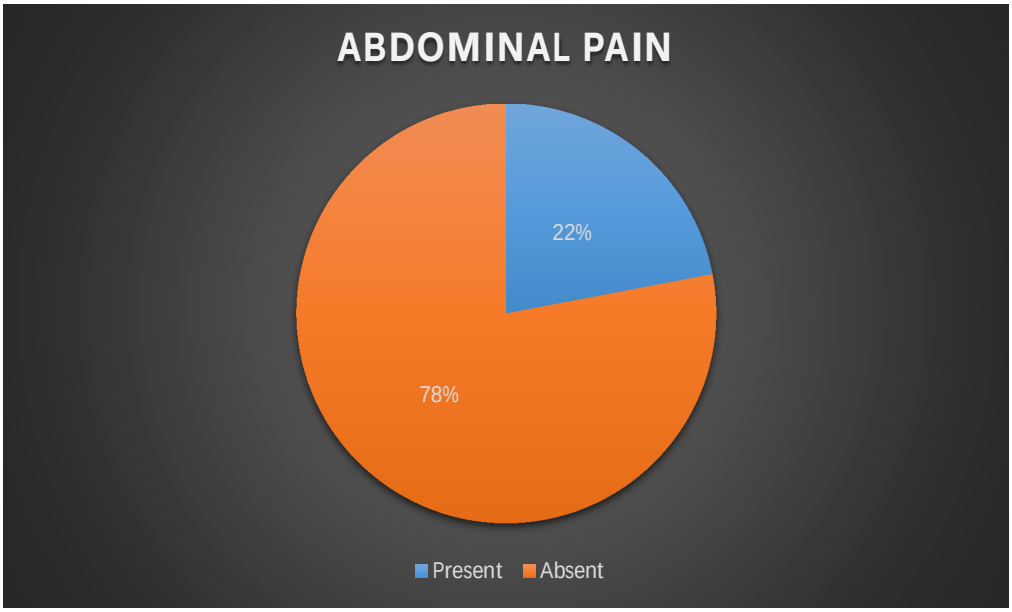
BLEEDING	NUMBER
Present	16(32%)
Absent	34(68%)

In this study, 16(32%) had bleeding and 34(68%) had no bleeding.



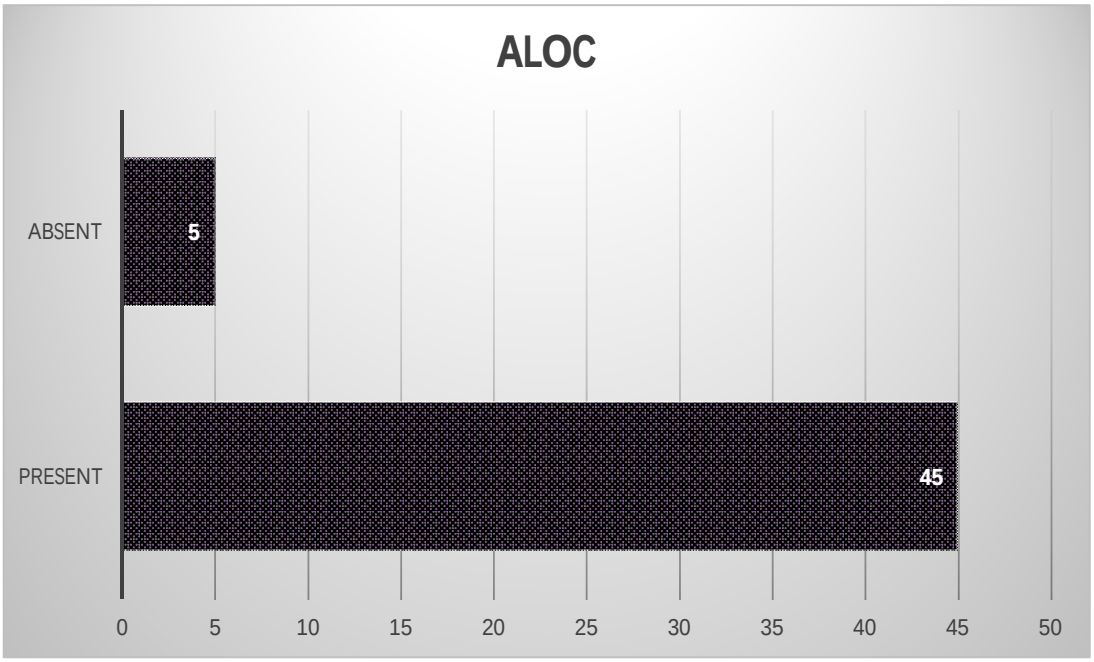
ABDOMINAL PAIN	NUMBER
Present	11(22%)
Absent	39(78%)

In this study abdominal pain was present in (22%) and absent in 78% of cases



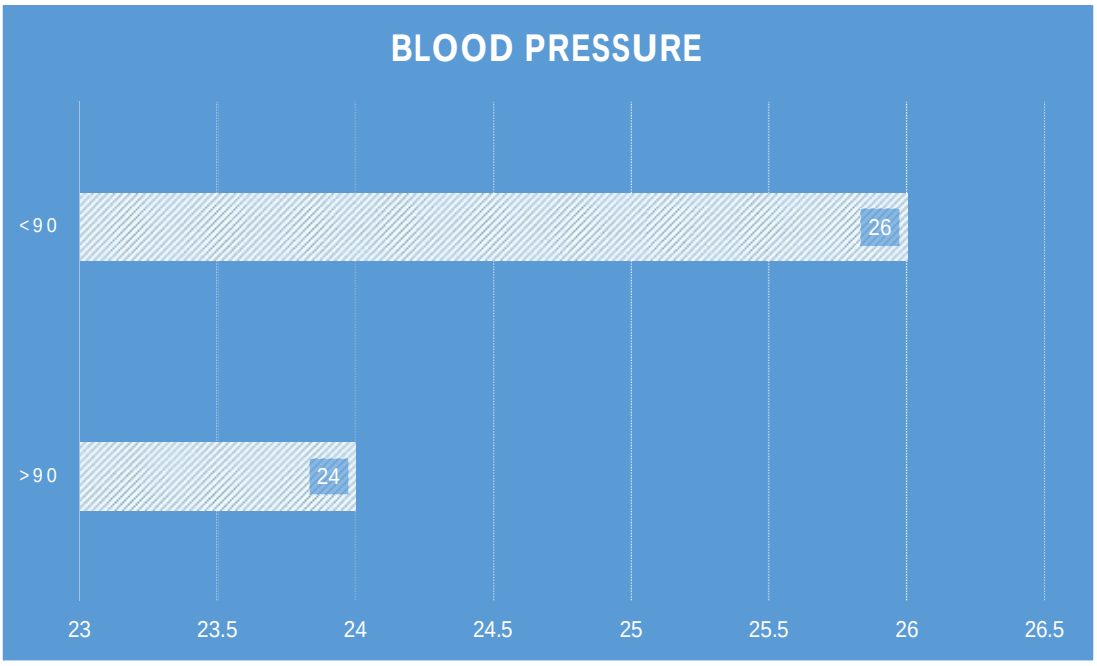
ALOC	NUMBER
Present	45(90%)
Absent	5(10%)

In this study 90% of the cases had altered level of consciousness and 10% of cases did not have altered level of consciousness



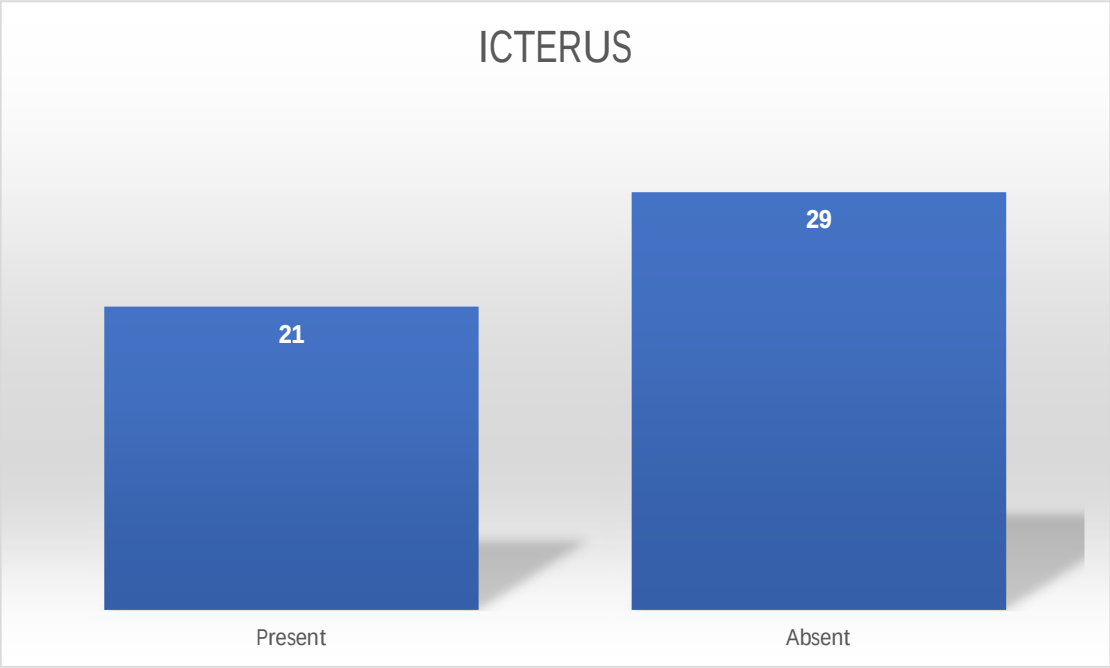
BLOOD PRESSURE	NUMBER
>90	24(48%)
<90	26(52%)

In this study, 24(48(%) had blood pressure >90 mm Hg and 26(52%) had blood pressure <90 mm Hg.



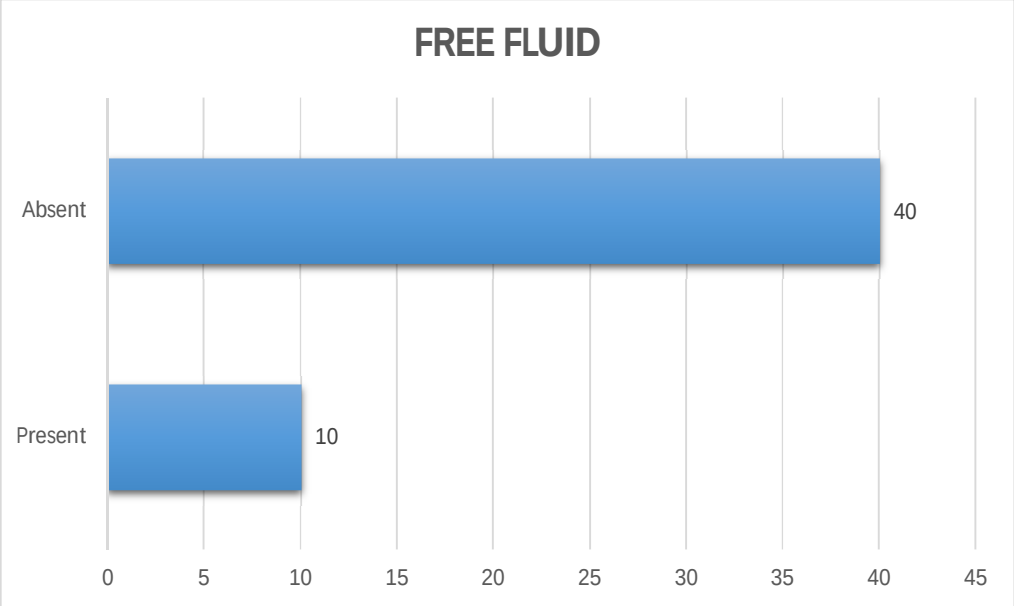
ICTERUS	NUMBER
Present	21(42%)
Absent	29(58%)

In this study, 21(42%) had icterus and 29(58%) didn't have jaundice.



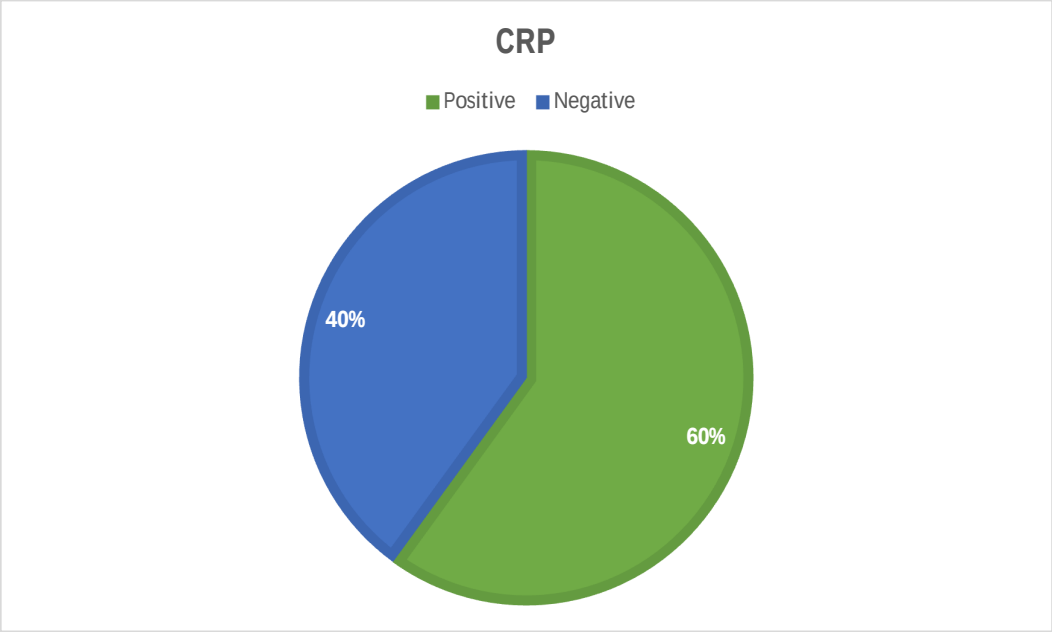
FREE FLUID	NUMBER
Present	10(20%)
Absent	40(80%)

In this study, 10 (20%) had free fluid detected by clinical examination.40 (80%) didn't have free fluid .



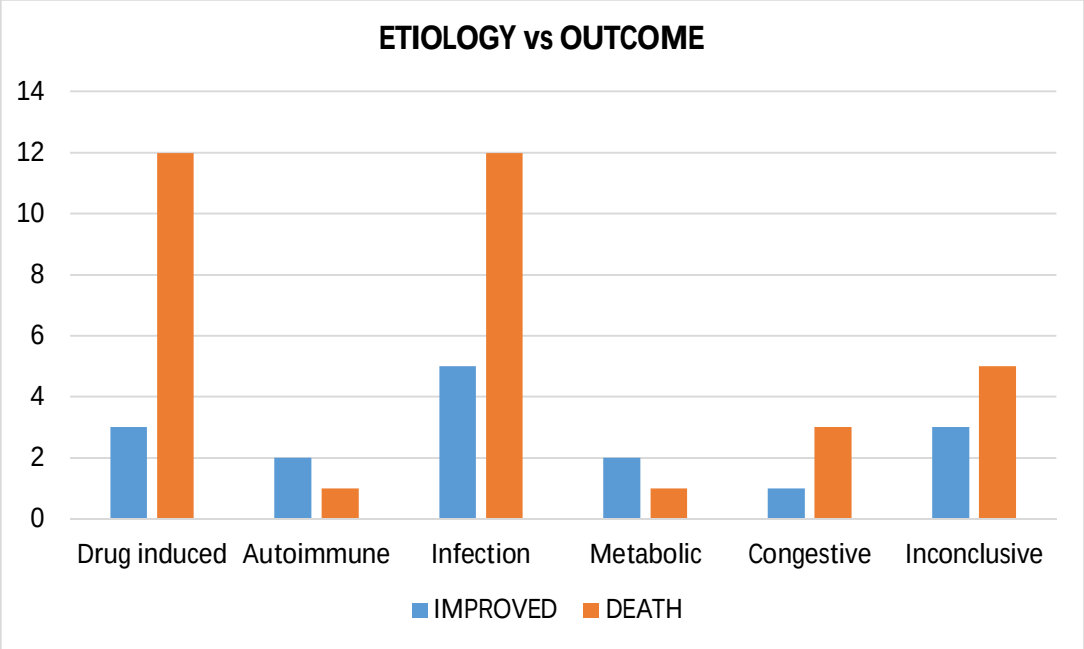
CRP	NUMBER
Positive	30(60%)
Negative	20(40%)

In this study, CRP was positive in 30(60 %) and negative in 20(40%).



S.No	Variable		Outcome		Chi square test (C)/ Fisher exact test (F) P value
			Improved	Death	
1.	Diagnosis	Drug induced	3	12(80%)	0.455 (F)
		Autoimmune	2	1(33%)	
		Infection	5	12(70%)	
		Metabolic	2	1(33%)	
		Congestive	1	3(75%)	
		Inconclusive	3	5(62%)	

In this study, among the causes drug induced had mortality of 80% followed by congestive(75%) infection (70%) inconclusive (62%) autoimmune (33%) metabolic(33%) P value was 0.4 so there was no association etiology and outcome.



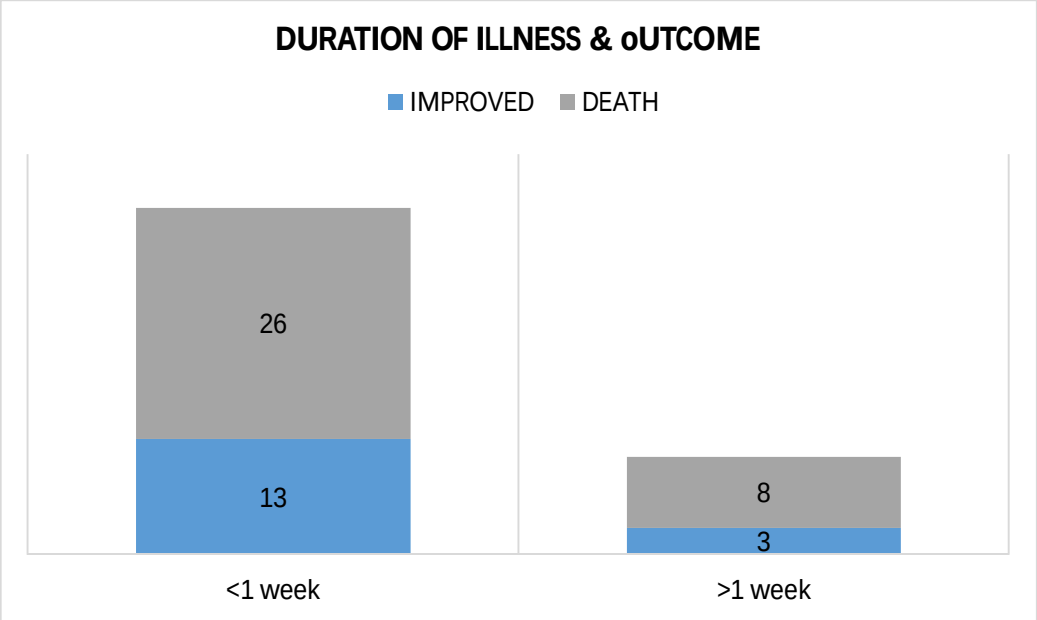
Association between bleeding and outcome

S.No	Variable		Outcome		Chi square test / Fisher exact test P value
			Improved	Death	
2.	Bleeding	Present	5	11	0.93 (C)
		Absent	7	27	

Association between duration of illness and outcome

S.No	Variable		Outcome		Chi square test / Fisher exact test P value
			Improved	Death	
3.	Duration of illness	<1 week	13	26	1.00 (F)
		>1 week	3	8	

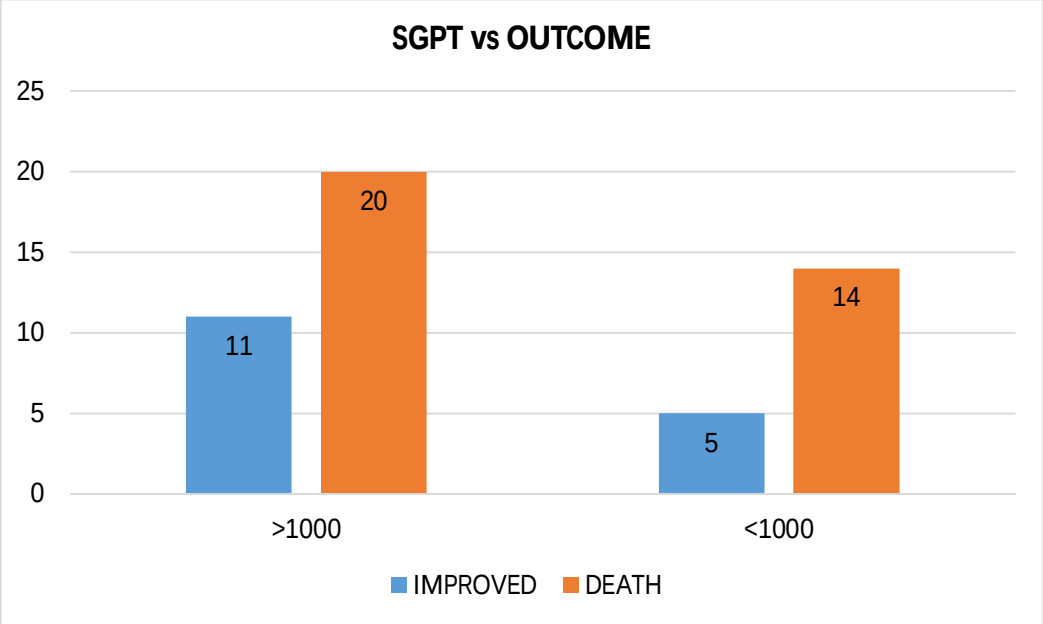
In this duration of illness was compared to the outcome.in cases with illness <1 week 26 cases died and 13 cases improved while in cases with illness >1 week 8 cases died and 3 improved.the P value was 1 hence there was no association between duration of illness and outcome



Association between PT and outcome

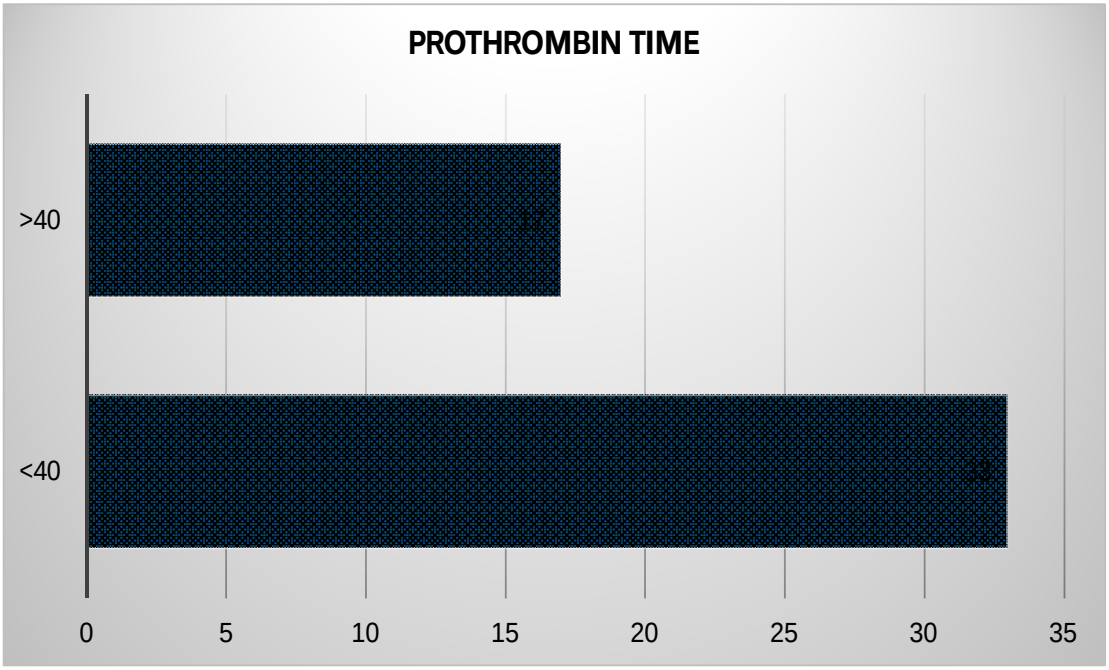
S.No	Variable		Outcome		Chi square test / Fisher exact test P value
			Improved	Death	
4.	SGPT	>1000	11	20	0.50 (C)
		<1000	5	14	

In this study SGPT value was compared with the outcome in cases with value <1000 twenty cases died while 11 cases improved.In cases with values >1000 14 cases died and 5 cases improved.The P value was 0.5 hence there was no correlation between SGPT values and outcome.



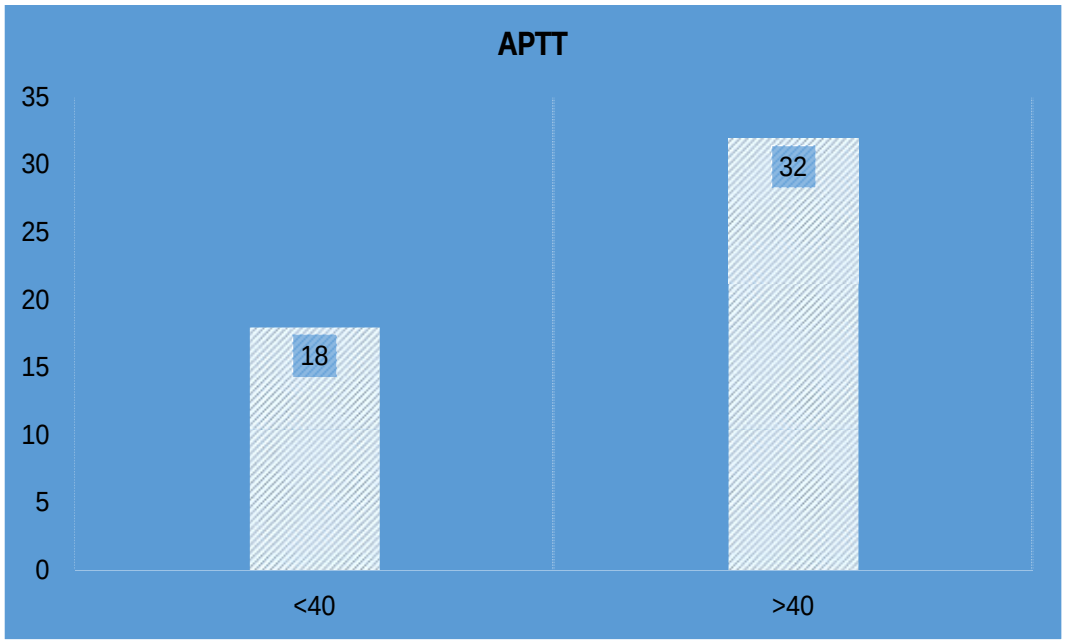
Prothrombin time	NUMBER
<40	33(66%)
>40	17(34%)

In this study, prothrombin time was <40 in 33(66%) and was <40 in 17(34%).



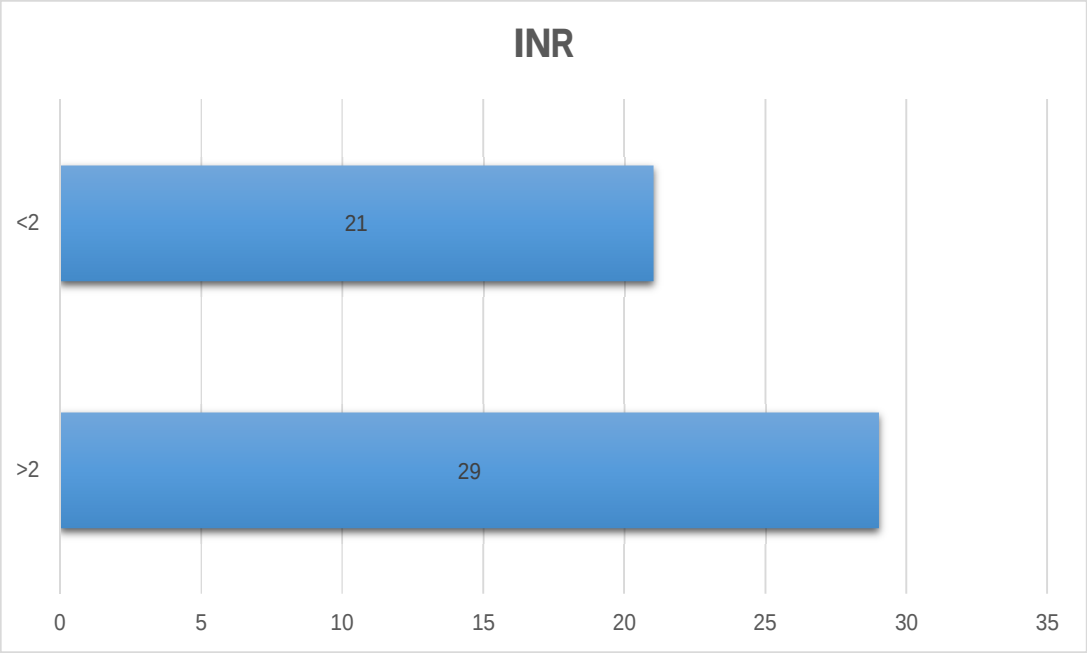
APTT	NUMBER
<40	18(36%)
>40	32(64%)

In this study, APTT was <40 in 18(36%) and >40 32(64%).



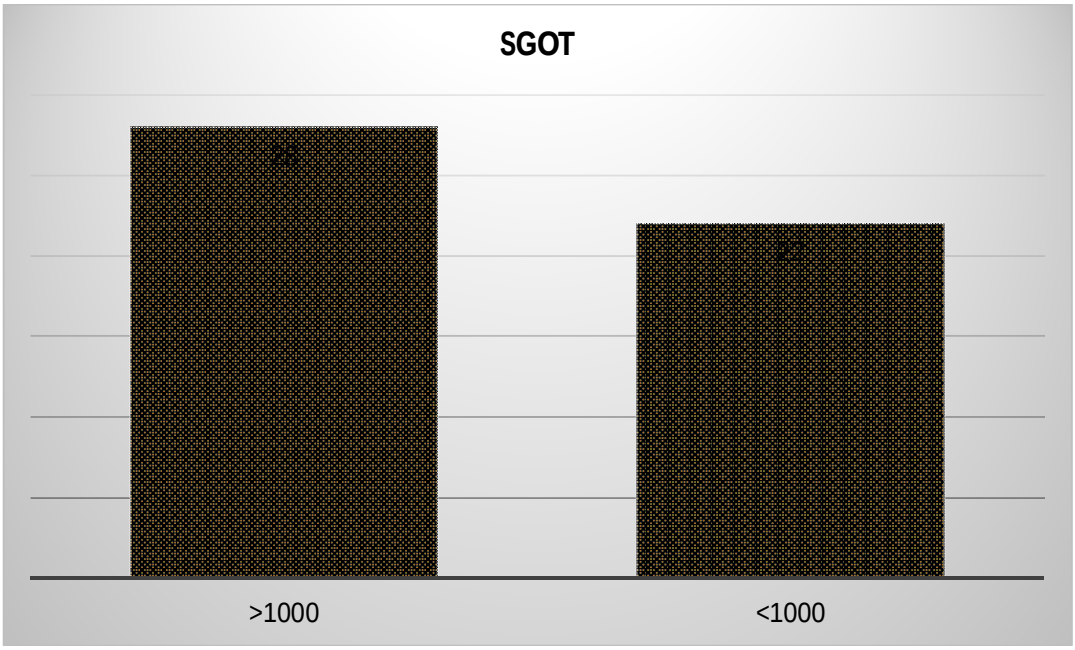
INR	NUMBER
>2	29(58%)
<2	21(42%)

In this study, INR was >2 in 29(58%) and INR was <2 in 21(42%).



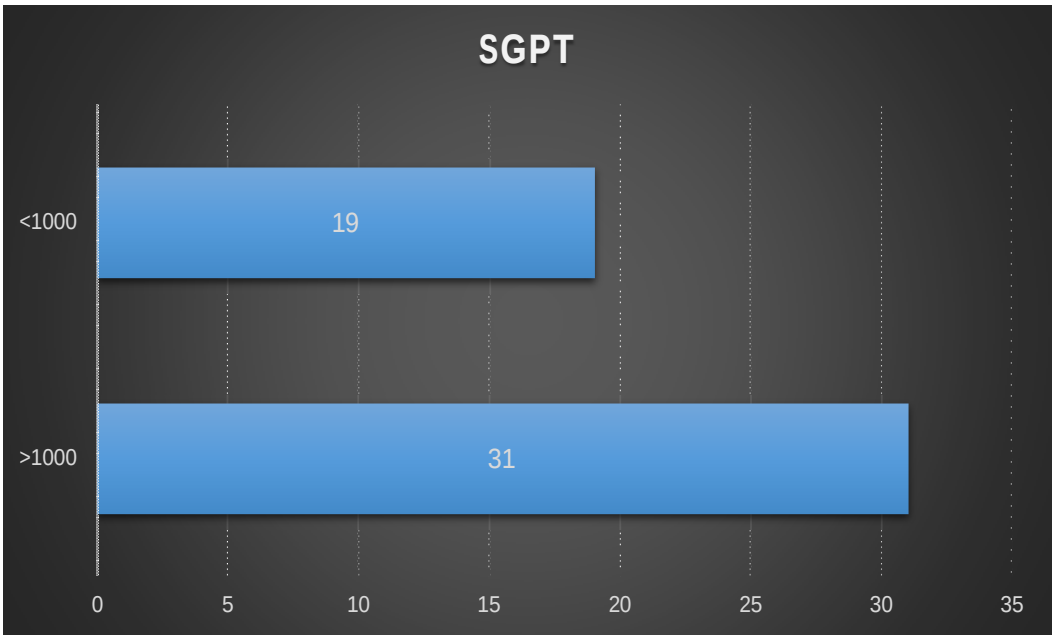
SGOT	NUMBER
>1000	28(56%)
<1000	22(44%)

In this study, SGOT was >1000 in 28(56%) and SGOT was <1000 in 22 (44%).



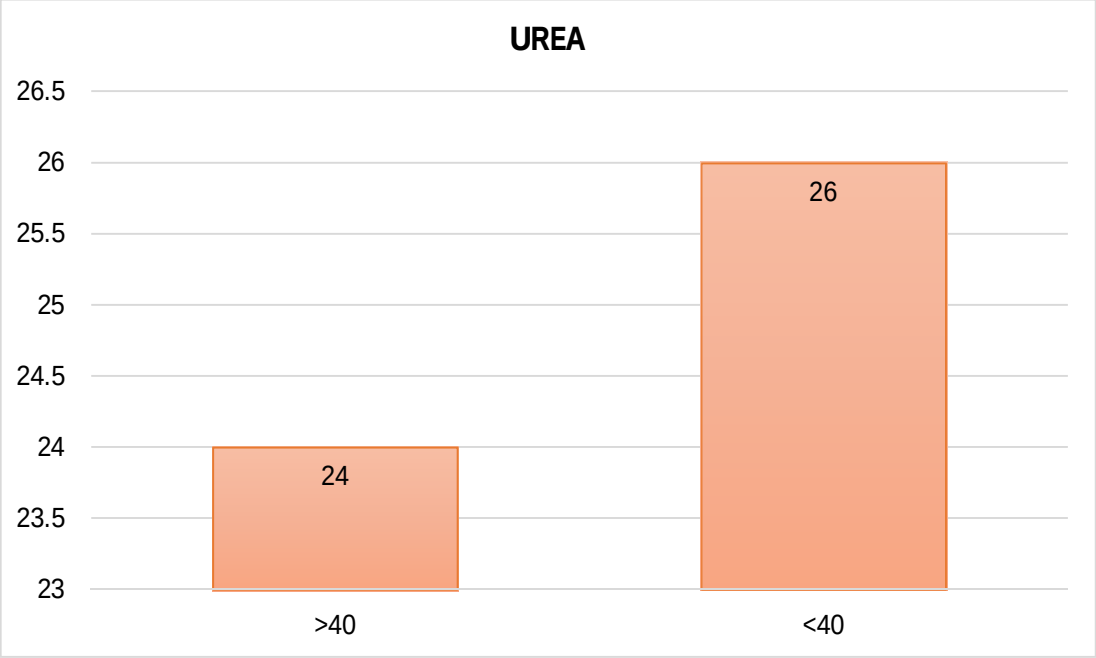
SGPT	NUMBER
>1000	31(62%)
<1000	19(38%)

In this study, liver enzyme SGPT was >1000 in 31(62%) and SGPT was <1000 in 19(38%).



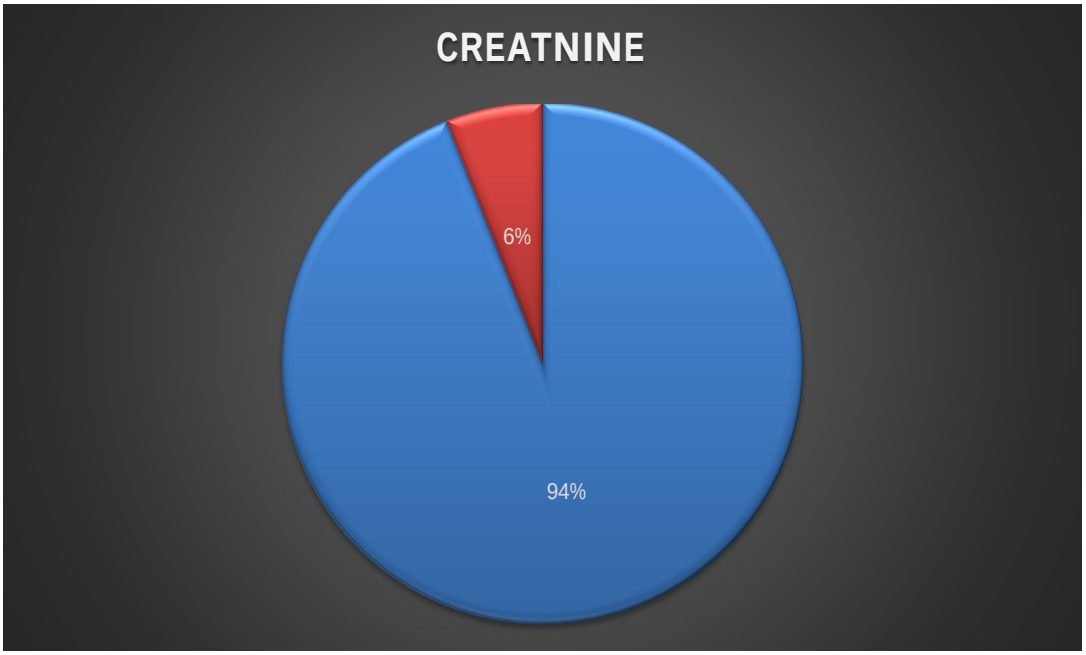
UREA	NUMBER
>40	24(48%)
<40	26(52%)

In this study, 24(48%) had urea >40 and 26(52%) had urea <40.



CREATININE	NUMBER
<3.5	47(94%)
>3.5	3(6%)

In this study, 47(94%) had creatinine <3.5 and 3(6%) had creatinine >3.5.



Discussion

DISCUSSION

AGE DISTRIBUTION

In this study among the 50 children studied the age distribution was found to be 42% of the children belong to 6-12 years, 36% belong to 1-5 years and 22% belong to <1 year group. This is comparable to kaur et al[70] in which 41.8% belong to 6-12 years ;44% belong to 1-5 years and 14% belong to <1 year In S Ganguly et al[73] age ranged from 2.8 to 12 years with mean age of 7.12 years

SEX DISTRIBUTION

In our study the sex distribution of acute liver failure was found to be 30(60%) of the children are females and 20(40%) are males. This is comparable to kaur et al[70] 70% are males 30% are females

ETIOLOGICAL PROFILE

In this study, out of the 50 children studied, 16(32%) improved and 34(68%) died. In this study, the etiology of liver failure was found to be infection(34%), drug induced(30%), idiopathic(16%), congestive causes(8%).

This is comparable to kaur et al [70]in which Infections were the most common cause (77%) with viral hepatitis (hepatitis A-E) in 72% cases. This is comparable to this study pediatric acute liver failure study group[71] in which etiology of acute liver failure in infants are found to be inderminate (38%),neonatal hemochromatosis(13.6%),herpes simplex virus (12.8%)

spontaneous survival occurred in 60% of infants 16% underwent liver transplantation and 24% died without undergoing liver transplantation[71]

O'Grady et al [73] argued for viruses other than hepatitis A and Bas bad prognostic markers, they documented that hepatitis E had the highest rate of mortality, the overall survival of ALF due to viral hepatitis was 40% while it was 25% for non A non B hepatitis in this study. Also khuroo et [al74] depicted that non E viral hepatitis as a predictor of poor outcome.

DURATION OF ILLNESS

In this study the duration of illness was found to be <1 week in (78%) and >1 week in (22%).

CLINICAL CORRELATION

In this study, 16(32%) had high coloured urine and 34(68%) didn't have high coloured urine.

In this study, 16(32%) had bleeding and 34(68%) had no bleeding. This is comparable to kaur et al[70] which 42% had bleeding and 58% did not have bleeding. In this study abdominal pain was present in (22%) and absent in 78% of cases In this study 90% of the cases had altered level of consciousness and 10% of cases did not have altered level of consciousness

In this study, 24(48(%) had blood pressure >90 mm Hg and 26(52%) had blood pressure <90 mm Hg. In this study, 21(42%) had icterus and 29(58%) didn't have jaundice.

In this study, 10 (20%) had free fluid detected by clinical examination.40 (80%) didn't have free fluid. In this study, CRP was positive in 30(60 %) and negative in 20(40%).

ETIOLOGICAL PROFILE AND OUTCOME

In this study, among the causes in drug induced 12 cases died 3 improved in infection 12 died 5 improved among autoimmune I died 2 improved among metabolic 2 cases improved 1 died among congestive causes 3 died and 1 improved and among inconclusive 5 cases died and 3 cases improved.P value was 0.4 so there was no association etiology and outcome .this is comparable to

DURATION OF ILLNESS AND OUTCOME

In this duration of illness was compared to the outcome.in cases with illness <1 week 26 cases died and 13 cases improved while in cases with illness >1 week 8 cases died and 3 improved.the P value was 1 hence there was no association between duration of illness and outcome In this study SGPT value was compared with the outcome in cases with value <1000 twenty cases died while 11 cases improved. In cases with values >1000 14 cases died and 5 cases improved. The P value was 0.5 hence there was no correlation between SGPT values and outcome.

LABORATORY

In this study, prothrombin time was <40 in 33(66%) and was <40 in 17(34%). In this study, 47(54%) had creatinine >3.5 and 3(6%) had creatinine <3.5. In this study, 24(48%) had urea >40 and 26(52%) had urea <40 In this study, liver enzyme SGPT was >1000 in 31(62%) and SGPT was <1000 in 19(38%). In this study, SGOT was >1000 in 28(56%) and SGOT was <1000 in 22 (44%). In this study, INR was >2 in 29(58%) and INR was <2 in 21(42%). This may be comparable with this study Etiology outcome and prognostic indicators of childhood fulminant hepatic liver failure in United kingdom[72]which found with an INR of 4 or more the mortality rate reaches 86% with an INR of <4 mortality is as low as 27%.

In this study, APTT was <40 in 18(36%) and >40 32(64%). In this study, prothrombin time was <40 in 33(66%) and was <40 in 17(34%).

Conclusion

CONCLUSION

1. In this study infection(34%) was the most common cause of acute liver failure followed by drug (30%)

2. In this study out of the 50 cases studied 68% died and 32% improved

3. Highest mortality was in the drug (80%) and congestive etiology(75%)

4. There was no correlation between demographic factors such as age sex and outcome

5. Our study failed to establish any association between clinical laboratory values and outcome

Since ALF is a potentially fatal condition, estimating the likelihood of spontaneous recovery and identifying patients who cannot be salvaged without liver transplantation is necessary. Prognostic factors that predict mortality and need for early liver transplantation are required. Our study results highlight the fact that viral hepatitis remains the most common cause of acute liver failure.

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Annexures

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI 600 003

EC Reg.No.ECR/270/Inst./TN/2013
Telephone No.044 25305301A
Fax: 011 25363970

CERTIFICATE OF APPROVAL

To
Dr.A.S.Vaanmathi
Post Graduate in MD Paediatrics
Madras Medical College
Chennai 600 003

Dear Dr.A.S.Vaanmathi,

The Institutional Ethics Committee has considered your request and approved your study titled **"CLINICAL PROFILE AND ETIOLOGY OF ACUTE LIVER FAILURE IN CHILDREN " NO. 15102016.**

The following members of Ethics Committee were present in the meeting hold on **04.10.2016** conducted at Madras Medical College, Chennai 3

1.Dr.C.Rajendran, MD.,	:Chairperson
2.Dr.M.K.Muralidharan,MS.,M.Ch.,Dean, MMC,Ch-3	:Deputy Chairperson
3.Prof.Sudha Seshayyan,MD., Vice Principal,MMC,Ch-3	: Member Secretary
4.Prof.B.Vasanthi,MD., Prof.of Pharmacology.,MMC,Ch-3	: Member
5.Prof.K.Ramasubramanian,MS, Prof. of Surgery,MMC,Ch-3	: Member
6.Prof.N.Gopalakrishnan,MD,Director,Inst.of Nephrology,MMC,Ch	: Member
7.Prof.R.Padmavathy, MD, Director,Inst.of Pathology,MMC,Ch-3	: Member
8.Prof.S.Mayilvahanan,MD,Director, Inst. of Int.Med,MMC, Ch-3	: Member
9.Tmt.J.Rajalakshmi, JAO,MMC, Ch-3	: Lay Person
10.Thiru S.Govindasamy, BA.,BL,High Court,Chennai	: Lawyer
11.Tmt.Arnold Saulina, MA.,MSW.,	:Social Scientist

We approve the proposal to be conducted in its presented form.

The Institutional Ethics Committee expects to be informed about the progress of the study and SAE occurring in the course of the study, any changes in the protocol and patients information/informed consent and asks to be provided a copy of the final report.

Member Secretary – Ethics Committee

MEMBER SECR.
INSTITUTIONAL ETHICS CO.
MADRAS MEDICAL COLLEGE
CHENNAI-600 003

INFORMATION SHEET

Place of study: INSTITUTE OF CHILD HEALTH AND HOSPITAL FOR CHILDREN,

Name of Investigator : .DR. VAANMATHI.A.S

Name of Participant	age:	sex:
Address:	Hospital No:	RC No:

We are conducting a study on **CLINICAL PROFILE AND ETIOLOGY OF ACUTE LIVER FAILURE IN CHILDREN**

We request you to participate in the study

- The purpose of this study is to find out the clinical profile and etiology of acute liver failure in children in our centre,ICH&HC
- To study clinical profile correlate with various etiology
- Clinical course, various complications & outcomes of acute liver failure in children can be studied. This will help us to inform the parents about the prognosis & treatment response.

• The privacy of the patients in the research will be maintained throughout the study. In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.

• Taking part in this study is voluntary. You are free to decide whether to participate in this study or to withdraw at any time; your decision will not result in any loss of benefits to which you are otherwise entitled.

.

Signature of investigator Signature of participant's Father / Guardian

Date:

ஒப்புதல் படிவம்

ஆய்வு எண்
பெயர் :
தேதி :

ஆய்வின் தலைப்பு : 1 மாதம் முதல் 12 வயது வரை உள்ள குழந்தைளின் கல்லீரல் செயலிழப்பின் நோய் காரணிகளும் மருத்துவ சுய விபரங்களும்.

நான் திருமதி..... எழும்பூர் குழந்தைகள் நல மருத்துவமனையில் சேர்ந்துள்ளேன். மருத்துவமனை எண்..... இடம் எழும்பூர்.

1 மாதம் முதல் 12 வயது வரை உள்ள குழந்தைளின் கல்லீரல் செயலிழப்பின் நோய் காரணிகளும் மருத்துவ சுய விபரங்களும். ஆய்வு பற்றி மருத்துவர் என்னிடம் எடுத்துக் கூறினார். இந்த ஆய்வின் தன்மை பற்றியும், பயன்களைப் பற்றியும் என்னிடம் மருத்துவர் தெளிவாக கூறினார்.

நான் இந்த ஆய்விற்கான ஒப்புதலை, இந்த ஆய்வு பற்றி முழுவதும் அறிந்தபின்பே அளித்தேன். இந்த ஆய்வில் எவருடைய வேண்டுகோளும் இல்லாமல் பங்கேற்கிறேன். நான் இந்த ஆய்வில் இருந்து எந்நேரத்திலும் விலகிக் கொள்ளலாம் என்பதையும் அதற்காக சிகிச்சை எந்தவிதத்திலும் தடைப்படாது என்பதையும் மருத்துவர் மூலம் அறிந்து கொண்டேன். நான் மருத்துவரின் கேள்விகளுக்கு பதிலளிக்க முழு மனதுடன் ஒப்புதல் அளிக்கிறேன்.

ஆய்வாளரின் கையொப்பம் ஆய்வில் பங்கேற்பவரின் கையொப்பம்

இடம் :

தேதி :

PROFORMA

NAME :

AGE :

PLACE :

IP NO :

DURATION OF ILLNESS :

FEVER :

JAUNDICE :

ABDOMINAL PAIN :

HIGH COLOURED URINE :

BLEED :

ALOC :

VITALS :

HR : BP :

LIVER SPAN :

FREE FLUID :

SPLEEN :

COMA SCALE :

HB :

TOTAL COUNT :

DIFFERENTIAL COUNT :

PERIPHERAL SMEAR :

LFT :

OT :

PT :

PT/APTT/INR :

TOTAL PROTEIN/ALBUMIN/GLOBULIN :

USG ABDOMEN :

CXR :

SERUM CERULOPLASMIN :

KF RING :

SERUM PARACETAMOL LEVELS :

UREA/CREATININE :

SERUM SODIUM/POTASSIUM :

OTHER INVESTIGATIONS :

TREATMENT :

MASTER CHART

name	outcome	diagnosis	address	age	age/sex	ip no	duration	fever	jaundice	high colored u	aloc	bleed	abdminal pain	drug	sensorium	bp	pulse	icterus	liver s/c	spleen	ff	hb	ps	tc	dc	crp	pt
devesh	improved	inconclusive	vandavasi	8 months	male	937227	7 days	2 days	present	no	yes 2 days	no	no	no	e4 v3m4	90/60	140	present	12cm firm	6cm	present	10.6		10300	57/43	negative	no coagulation
jaffrin fathima	improved	paracetamol toxicity	adayar	3	female	937818	5 days	5 days	no	no	2 days	no	no	paracetamol	letargic	98/70	100	no	no	no	present	10.7		6370	67/33	positive	30.5/31/2.28
ankitha das	improved	autoimmune hepatitis	tripura	11	female	937024	4 days	no	20 days	no	3 days	no	no	no	e3v3m5	110/70	90	present	10cm firm	no	no	12.5		9800	56/39/5	negative	36/42/3.43
aaron	improved	leptospirosis	chennai	3	male	934786	1 day	1 day	1 day	no	1 day	hematuria	no	no	e1vtm1	100/70	120	present	10cm firm	3cm	no	3.2	features suggestive of hemolytic anemia	18300	62/31/7	positive	24.7/27.7/2.37
monalisa	death		nerkundram	10	female	936072	2 days	2 days	2days	no	2 days	no	no	valproate	e1vtm1	120/90	118	present	6cm soft	no	no	10		1600	67/23/10	negative	58.9/0.8/5.1
sibikashree	death	paracetamol toxicity	vellore	2	female	925127	7 days	7 days	2 days	2 days	1day	hematemesis 1 episodemalena 1 episode	no	paracetamol	e1v1m4	96/62	130	present	5.5cmfirm	no	no	9.4		9399	70/19/11	positive	110/50.6/9.88
ajith	death	hepatitis A	bihar	3	female	875887	1 month	4 days	1month	1 month	3 days	no	no	native medication	e1vtm1	100/70	96	present	8cm firm	no	no	7.7	moderate anispoikilocytosis platelet in single and good clumps	19400	64/36	positive	58.5/78.6/4.5
lakshana	death	sepsis	vellore	2	female	880577	10 days	10 days	7 days	7 days	1 day	no	no	native medication	e2v1m4	100/70	120	present	8cm firm	no	no	12.2		36000	66/34	positive	38/36.6/3.2
dinesh kumar	death	inconclusive	kadappa	2	male	921613	3 weeks	3 weeks	2 weeks	2 weeks	5 days	no	no	no	e1vtm1	90/60	130	present	10cm firm	no	no	7.9		8100	71/22/07	negative	>120/>120 inr 5.2
ashwin	death	paracetamol toxicity	kk nagar	6	male	925435	6 days	6 days	no	no	1 day	hematemesis 1 episodemalena 1 episode	no	paracetamol 110mg/kg	e1vtm1	100/70	130	no	8cm firm	no	no	9.5		11300	81/14/0	negative	13.2/47.8/2.59
pooja	death	inconclusive	vyasarpadi	6	female	928793	10 days	10 days	10 days	2 days	2 days	no	no	native medication	e2v3m4	100/70	120	present	9cm firm	no	no	10	netrophillia with hypersegmented neurophils	19400	85/9/6	positive	27.6/29/2.72
sahasara	death	autoimmune hepatitis	choolaimedu	2	female	884515	1 month	no	1 month	1 month	4 days	no	no	no	e2v1m4	90/60	110	present	7cm firm	no	no	6.4	anemia with thrombocytopenia	9600	71/21/8	positive	41/36/4.5

shaek amrin	improved	drug induced	andhra pradhesh	5	female	937255	20 days	10 days	6 days	6 days	6 days	hematuria	no	adriamycin vincristine cyclophosphamide	e4v2m	100/60	110	present	8cm firm	no	no	5.7		4000	93/6/1	negative	100/42/9
b/o lakshmi	death	tyrosinemia	andhra pradhesh	3 months	male	938302	9 days	no	9 days	9 days	7 days	malena 1 episode	no	no	e4v2m5	90/50	140	present	7cn firm	8cm firm	no	9.3	normoctic normochromic anemia with thrombocytopenia	3300	39/59/11	positive	22.7/70/2
munihema varshini	death	PFIC	andhra pradhesh	2	female	922107	15 days	2 days	15 days	15 days	2 days	no	no	no	e1vtm1	110/70	160	present	7cmfirm	no	present	12	hypochromic anisocytosis platelet in single clumps	21200	56/39/5	positive	17.6/47.8/1.53
annaporani	death	sepsis	thanjavur	11	female	932092	2 days	no	2 days	2 days	2 daays	no	no	no	e1vtm1	120/90	130	present	11cm firm	4cm	no	7.2	moderate anispoikilocytosis platelet in single and good clumps	17500	67/26/6	positive	26.4/36.8/2
anbarasi	improved	sle	salem	9	female	937120	20 days	20 days	4 days	no	2 days	no	3 da	azathioprine	e3v3m5	100/70	110	no	7cm normal	no	no	12.8	microcytic hypochromic anemia	11300	87/10/3	positive	83.4/56/7.07
jeyarani	death	paracetamol toxicity	chennai	1	female	937792	7 days	7 days	no	no	1 day	hematemesis 1 episode	no	paracetamol	e1vtm1	74/42	150	no	7cm firm	no	no	9.4		2800	32/68	positive	62/49/1.59
sivasakthi	death	wilson/hepatitis A	kallakurichi	9	male	939585	3 days	3 days	3 days	3 days	1 day	hematuria	3 days	no	e1vtm1	130/60	130	present	12cm firm	2cm	present	3.6		39500	76/20/4	negative	26/44/3.3
muthuselvam	improved	congestive hepatic failiure/hepatitis B	kumbakonam	9	male	939331	5 days	no	4 days	no	no	no	5 days	no	e3v3m5	90/60	100	present	10cm firm	no	no	8.2		24500	85/15	positive	39.1/34/3.31
thanuja barla	death	congestive hepatic failiure	andhra pradhesh	10	female	940777	1 week	ni	no	no	3 days	no	no	no	e4v3m3	92/46	110	no	8cm firm	no	present	6.1		22700	60/40	negative	40/68/3
daniel	death	paracetamol toxicity	chennai	1	male	942877	4 days	4 days	no	no	1 day	hematemesis	no	paracetmol	e1vtm1	130/90	100	no	9cm firm	no	no	5.3		8100	76/21/3	positive	85/48/11.5
thugilan	death	paracetamol toxicity	kanchipuram	6 months	male	942762	3 days	3 days	no	no	1 day	no	no	paracetamol	e1vtm1	90/50	140	no	9cm firm	no	present	5.6		2600	35/4/11	positive	26.2/29.3/2.56
abiju	improved	dengue	chennai	9	male	943230	7days	7 days	3 days	1 day	no	no	no	no	e1vtm1	90/50	120	no	8cm soft	no	no	9.5	mild hypo mild anisocytosis	16400	83/10/7	positive	21.7/29.3/1.79
kaviyapriya	death	paracetamol toxicity	arani	6	female	942324		3 days	no	no	1 day	no	no	paracetamol	e1vtm1	110/70	139	no	8cm soft	np	present	10.1	mild hypo mild anisocytosis			positive	12.6/43/6.48
yasika	death	dengue	thiruvallur	2	female	944422	5 days	5 days	no	no	3 days	no	no	no	e1vtmi	80/50	130	present	8cm firm	no	present	9.6	mild hypo mild anisocytosis	26700	50/44/6	positive	37.2/no coagulation/2.76
kavinaya	death		thiruvallur	6	female	946488	2 days	1 day	no	no	1 day	hematemesis4 episodes	3 days	no	e1vtm1	80/40	138	no	6,5cm firm	no	no						
surendar	death	paracetamol toxicity	chennai	7	male	944898	4 days	4 days	no	no	1 day	no	3 days	paracetamol	e3v3m5	120/80	120	no	7cm soft	no	no	8.7		6600	62/34/4	positie	34/54/1.8
yathiran	death	inconclusive	thiruvarur	2	male	948422	7 days	7 days	7 days	no	5 days	NO	No	no	e4v3m6	100/70	115	yes	8cm soft	no	no	9.4	moderate anispoikilocytosis platelet in single and good clumps	16000	75/17/8	positive	50.4/no/4.49

roobesh kumar	improved	congestive hepatic failiure	vellore	12	male	948437	6 days	6 days	no	no	2 days	no	no	no	e4v5m5	80/50	110	no	8cm firm	no	no	11.3		22600	83/10/7	negative	19.3/40.2/1.6
ragini	death	rat killer poisoning	kanchipuram	5	female	948938	no	no	no	no	1 day	hematemesis	no	rat killer poison	e1vtm1	80/50	140	no	7cm soft	no	no	10.8	moderate anispoikilocytosis platelet in single and good clumps	6800	71/20/9	negative	160/90/9
sreenathi	death	inconclusive	arani	3	male	94970	5days	5 days	no	no	1 day	no	no		e1vtmi	90/60	110	no	7cm soft	no	no	7.4	severe to moderate hypochromic aniso poikilocytosis platelet in clumps	8400	50/34/16	positive	23/46/1.8
benson	improved	dengue	chennai	1	male	951528	4 days	4 days	no	no	1day	no	no	no	e4v5m5	80/60	160	no	9cm soft	no	present	9.9		18300	33/6/11	positive	21/39,4/1.78
masquad asan	improved	hepatitis A	chennai	12	male	951598	8 days	8 days	7 days	7days	1 day	hematemesis	7 days	no	e4v3m6	110/70	100	present	8cm soft	no	no	10.2		9500	60/31/9	positive	12.6/54/1.54
tejasri	improved	inconclusive	vellore	2	female	951576	3 days	3 days	no	no	2 days	no	no	no	e4v3m4	80/50	120	no	10cmsoft	no	no	11.3		7800	50/44/6	positive	43/68/1.68
karthiga	death	sepsis	thiruvannamalai	1	female	950799	5 days	5 days	no	no	2 days	hematemesis	no	no	e1vtm1	60/40	130	no	8cm soft	no	no	8		36400	86/14	negative	32.1/68.7/2.88
ijayasarathi	improved	dengue/leptospirosis	chennai	9	male	950223	5days	5 days	no	no	no	hematuria	no	no	e4v3m4	110/80	70	no	8cm soft	no	no	10.6		3800	46/41/13	negative	13.9/36/1.53
nisha	death	dengue	chennai	5	female	949924	4 days	4 days	no	no	2 days	no	no	no	e1vtm1	70/60	100	no	7cm soft	no	no	13.6		11700	70/30	positive	38/46/1.98
sujatha	death	dengue	chennai	10	female	950374	5 days	5 days	no	no	2 days	no	1 day	no	e3v4m4	90/60	140	no	9cm soft	no	no	10.9		10200	53/47	negative	34/54/1.7
roshan	death	paracetamol toxicity	chennai	4	male	952202	4 days	2 days	no	no	3 days	no	1 day	paracetamol	e1vtm3	70/50	140	no	9 cm firm	no	no	12.7		15700	82/18	positive	45/68/6.8
rudhresh	death	dengue	kanchipuram	4	male	953281	5 days	5 days	no	no	1 day	hematemisis	3 days	no	e1vtm3	60/30	160	no	10 cm soft	no	no	6.5		23000	47/65/29	negative	42/58/4.2
jayamurugan	death	paracetamol toxicity	vellore	10	male	946927	3 days	3 days	3 days	2 days	1 day	no	3 days	paracetamol	e1vtm2	110/60	110	no	8 cm soft	no	no	7.2		7300	60/34/6	positive	20/47/16
samshika	death	paracetamol toxicity	chennai	11 months	female	942137	3 days	3 days	2 days	no	1 day	no	no	paracetamol	e4vtm5	70/40	140	present	9cm soft	no	no	5.8		17700	80/20	positive	11.2/111/no coaglation
monisha	death	inconclusive	krishnagiri	2	female	950769	20 days	20 days	3 days	no	3 days	no	no	no	e2v3m4	90/60	180	no	12cm firm	spleen tip palpable	present	7.5		23300	75/25	positive	15.9/34.1/1.62
kavishri	death	dengue	chennai	1	female	934968	5 days	5 days	5 days	2 days	2 days	no	no	no	e1vtm1	100/80	110	no	8 cm firm	spleen tip palpable	no	8.6		2500	34/47/19	negative	45/62/2.2
nivedhan	improved	metabolic	thiruvallur	3 months	male	952354	7 days	no	7 days	3 days	7 days	hematemesis malena	no	no	e3v5m5	90/60	140	present	8 cm firm	spleen tip palpable	no	8		21200	66/31/3	negative	102.1/28.7/6.9
kenisha	death	dengue	chennai	9	female	952804	7 days	7 days	no	no	2 days	hematemisis	2 days	no	e1vtm1	90/70	140		12 cm firm	no	no	12.7		34200	79/17/4	negative	21.7/12.2/1.86
madhuvanthani	improved	paracetamol toxicity	chennai	8 months	female	948451	7 days	7 days	no	no	1 day	no	no	paracetamol	e3v4m5	90/60	120	no	6.5 soft	no	no	11.1		9500	61/39/2	positive	32/48/1.58
vaideki	death	dengue	chennai	12	female	948934	5 days	5 days	no	no	no	no	no	no	e1vtm1	100/70	120		7 cm soft	no	no	10.1		7500	70/30	negative	44/56/2.2
charulatha	improved	hepatitis A	chennai	9	female	950346	5 days	5 days	no	no	no	no	no	no	e3v5m5	70/40	130		8cm soft	no	no	11		8500	84/16	negative	24/43/1.6

tbr/dbr	ot	pt	sap	protien al	sg abd	viral markers	wilson	kf ring	cerla plasmin	treatment	xray	other	s paracetamol	duration of stay	urea	creatinine	sodium	pottasium
5/2.7	268	164		4.1/2.6/1.5	hepatomegaly increased echoes spleen normal	negative	no	no		oxygen hepatic fluid vitamink syruplactulose ijection ampicillin tablet udca tab spironolactone	right pleural fluid	triglycerserum amylase10 serum lipase 44ide 1820 dengue igm negative,serum ammonia 58			22	0.5	136	4
1.5/1.4	6700	4300		4.7/2.9	hepatomegaly mild free fluid abdomen			no		oxygen hepatic fluid,injection n-acetyl cystiene,inj.vitamk,tab udca			7		17	0.6	137	3.2
11.2/9	1028	958	325	4.2/2.4	liver coarse increased echoes,no free fluid	negative	no	no	19	hepatic fluid inj.vitamin k lactulose,inj pantoprazole,tab udca ffp transfusion,inj.methylprednisolone	normal	anca positiveLKM antibody ANA positive cmv negative DCT positive ant SMA negative			25	0.7	145	4
10.7/0.7	223	33	129	5.6/3.6/2	hepatomegaly,reactive gb wall edema no ff spleen 8cm	negative	no			mechanical ventilation hepatic fluid crystalline penicillninj. artesunatePRBC transfusion,vitamin k syrup lactulose,n acetyl cysteine infusion	normal	LDH 2280 CPK 20307 QBC negative Retic count 4% MSAT 4+			76	0.5	132	5.1
20/8.3	748	1108	421	5.7/3.2		positive		no		mechanical ventilation hepatic fluid adrenaline infusion,vancomycin,amikacin,vitamin k syrup lactulose,n acetyl cysteine infusion		blood culture pseudomonas scrub typhus negative,leptospirosis negative			15	0.5	168	2.5
4/1.6	15900	7882		5.1/3.6	hepatomegaly no freefluid		no	no		oxygen,inj.cefotaxim,inj.n acetylcysteine,syrup lactulose,inj.vitamink inj.pantoprazole FFP transfusion			16		60	1.3	172	4.6
22/8.9	652	433		5.9/3.3/2.6	hepatomegaly reactive cholecystitis portal radicals appear prominent mild spleenomegaly minimal freee fluid abdomen	HAV positive	no	no	40	mechanical ventillation hepatic fluid FFP transfusion tablet udca inj.ampicillin,inj.dopamine inj.ranitidine	cardiomegaly congestion	MAT positive widal negative,NEC no growth,			17	0.5	136	4.4
11.7/6	907	2028	389	5.1/3./1.6	mild hepatomegaly liver echoes diffusely altered spleen normal no free fluid	negative	no			hepatic fluid inj.vitamin k lactulose,inj pantoprazole,tab udca ffp transfusion,inj.n acetyl cystine,inj.mannitol	normal	ammonia 483,lactate 1011,cpk 119			30	0.5	140	5.4
18.5/7.8	403	572		5.7/3.8	thickened edematous Gbwall ?secondary to acute viral hepatitis	negative	no			mechanical ventillation hepatic fluid FFP transfusion tablet udca inj.ampicillin,inj.dopamine inj.ranitidine	bilateral hyperinflation	MAT negative NEC no growth			14	0.4	145	3.7
2.6/1.4	14486	6312		6.2/4/2.2	heoatomegaly increased echoes spleen normal no free fluid	negative				mechanical ventillation hepatic fluid FFP transfusion tablet udca inj.ampicillin,inj.dopamine inj.ranitidine inj. N acetyl cystiene	normal	scrub typhus negative,dengue igM negative	,serum acetaminophen 46.9(10-30)		112	2.1	141	3.3
4.4/2	4370	3020		49/2.8/2.1	normal study	negative			27	oxygen hepatic fluid vitamink syruplactulose ijection ampicillin tablet udca inj.n acetylcystiene,FFP transfusion	cardiomegaly congestion	NEC klebsiella grown			97	2.4	132	4.7
18.7/8.2	294	192	384	6/3/2003	liver shows corse teture surface nodular multiple hyperechoic nodules on right lobe spleen normal	negative			45	oxygen	suggestive of ARDS	Anti LKM ab positive , MAT DFM positive			34	0.6	145	2.4

5.3/3	6792	2093	107	3/1.5/1.5	rhabdomyosarcoma bladder liver normal spleen normal minimal free fluid abdomen	negative		no		oxygen hepatic fluid inj.n acetyl cystine inj.pantoprazole FFP transfusion inj.dopamine,tab UDCA					98	1.6	133	4
6.1/4.9	4138	1448	200	4.8/2.9/1.1	liver 9cm enlrged in size altered echotexture GB partially distented Gbwall edema noted spleen 9.5cm enlarged mild free fluid portal vein 7mm	negative	no			oxygen	normal	lactate 9.9 ammonia105 GGT 29 alpha fetoprotein 125			53	0.4	143	3.1
13.6/6.5	105	39		5/2.7/2.3	hepatomegaly gall bladder wall thickrening moderate ascites mild spleenomegaly	negative				mechanical ventilation hepatic fluid dopamine cefotaxim ffp vitamin k	cardiomegaly congestion	widAL NEGATIVE MSAT NEGATIVE liver biopsy progressive familial intrahepatic cholestasis			52	0.8	145	4.2
9.8/4.5	74	39		7.1/3.6/2.5	hepatomegaly increased echoes spleen 12cm no free fluid portal vein 0.8 cm	negative				mechanical ventilation hepatic fluid udca lactulose	normal	dct negative ammonia59 LDH 981		2 DAYS	42	1	166	4.2
<1	38230	664		4.6/2.7/1.9	hepatomegaly minimal free fluid no pleural fluid	negative				inj piptaz syrup lactulose tab udca inj vitamin k ffp tab prednisolone inj acyclovir	normal	ANA speckled 3+ anti ds DNA positive			15	0.3	136	3.6
<1	14645	8250		5.6/3.8/1.8	hepatomegaly no freefluid	negative				mechanical ventilation inj nacetyl cystine dopamine oseltamivir	left lower lobe pneumonia				80	0.8	138	4.4
39.3/13	135	300		5.9/3.8/2.1	liver echoes normal spleenomegaly ascites	negative	yes	present	22	mechanical venti;lation	normal	24 hor rinary copper 274		5 days	97	1.2	136	5.1
5.6/2.3	58	386		4.8/2.6/2.2	ascites right kidney 8.8cm grade 1 rpd left kidney 8.6cm sleen normal	hbsag positive			33	dobutamine inj cefotaxim syrup lactulose tab udca metronidazole carnitine	cardiomegaly	echo severe LV dysfunction dilaed cardiomyopathy			114	1.4	128	2.4
4.1/2.1	224	120		5.5/2.9/2.6	congestive hepatomegaly minimal ascites	negative	no	no		dobutamine inj cefotaxim syrup lactulose tab udca metronidazole carnitine	cardiomegaly	echo severe LV dysfunction dilaed cardiomyopathy			36	1	128	4.4
1.4/0.6	11826	6936		5/3.5/1.5	hepatomegaly liver echoes increased gb wall edema		no	no		mechanical ventilation dopamine adrenaline n acetyl cystine vitamin k pantoprazole ffp prbc			26		61	0.8	125	5.8
1.2/0.8	3879	4817		4.1/3.6/0.5	hepatomegaly free fluid		no	no		mechanical ventilation dopamine adrenaline n acetyl cystine vitamin k pantoprazole ffp prbc	normal		38		104	1.5	153	5.3
<1	1977	1947		5.4/2.9	hepatomegaly minimal free fluid	negative	no			m	cardiomegaly right pleural fluid	dengue positive mat negative						
3.1/2	>10,000	5419		4.5/2.6	hepatomegaly reactive gb wall edema free fluid present	negative	no			mechanical ventilation adrenalne dopamine ffp ceftrioxone azithromycin vitamin k	normal		58		84	3.8	144	5.4
2.9/0.6	683	2832		4/2.9/1.1	hepatomegaly reactive gb wall edema free fluid present	negative	no			mechanical ventilation adrenalne dopamine ffp ceftrioxone azithromycin vitamin k	bilateral pleural fluid	lactate 92 cpk 70 ldh 728		5 days	43	0.8	132	4.7
<1	2418	422		5.4/3.6/1.8	hepatomegaly gb wall edema no pleural fluid	negative	no	no		mechnical ventillation dopamine ffp hepatic fluid	bilateral pleural fluid	DFM Negative MAT negative scrub negative	3.3		16	0.7	128	3.6
2.1/0.6	137	435	333	4.3/2.9/1.6	features suggestive of hepatitis no spleenomegaly no ascites	negative	no	no		udca viatamin k hepatic fluid lactulose enema	normal	lactate 6.7 ldh 1068 ammonia 41 alpha fetoprotein 26		7 days	17	0.5	137	4.2

<1/	492	754		6/3.2	hepatomegaly no free fluid	negative	no	no		udca viatamin k hepatic fluid lactulose enema	normal	echo severe MR severe AR RHD		6 days	60	1.2	132	4.3
4.8/2.5	6095	2427		5.4/3.8/1.8	mild hepatomega;y no free fluid	negative	no	no		mechnical ventillation dopamine ffp hepatic fluid	normal			1 day	44	2.3	132	2.5
2.9/1.6	8813	2024		5/3.4/1.6	hepatomegaly no freefluid	hepatitis A positive	no	no		mechnical ventillation dopamine ffp hepatic fluid	normal	MAT positive		5 days	97	3.9	135	5.2
<1	1588	541		5.4/2.9/2.3	mild hepatomegaly gall bladder wall edema right pleural fluid no free fluid abdomen	negative	n o	no		mechnical ventillation dopamine ffp hepatic fluid	normal	dengue positive		4 days	18	0.5	135	4.5
9.9/3.3	786	982		7.1/3.8/3.3	liver normal spleen normal no free fluid	hepatitis A positive	no	no		hepatic fluid tab udca inj.vitamin k lactulose syrup	normal	widal negative		8 days	15	0.6	135	5.1
<1	7745	5752	203	4.8/2.8/2	mild hepatomegaly o free fluid no pleural fluid		no	no		hepatic fluid tab udca inj.vitamin k lactulose syrup	pneumonitis both lower lobe	MAT negative denguenegative		3 days	18	0.6	132	4.6
<1	366	119		4.7/3.3.1.4	mild hepatomegaly no free fluid	negative	no	no		mechnical ventillation dopamine ffp hepatic fluid	normal	lactate 115		5days	132	2.7	145	6.1
<1	138	99		3.7/2.8/0.7	mild hepatomegaly gall bladder wall edema right pleural fluid no free fluid abdomen	negative	no	no		hepatic fluid tab udca inj.vitamin k lactulose syrup	bilateral pleural fluid	DFM positive dengue positive		5 days	16	0.4	138	3.5
<1	234	333																
<1	2063	698																
4.4/3.5/0.5	16300	6600	183	4.7/2.6/2.1	hepatomegaly	negative	no	no		hepatic fluid tab	pneumonitis R lower lobe		37	5 days	28	1	112	4.6
<1	1865	466		43/2.5/1.8	hepatomegaly no free fluid	negative	no	no			Right pleural fluid	igM dengue positive		5 days	58	0.6	131	4.3
11.1/4.4	350	250	28	4.5/2.8/1.7	hepatomegaly moderate free flid	hepatitis A	no	no			normal				177	3.2	140	4.2
8.7/4.4	247	650	166	4/2.9/1.1	hepatomegaly no free fluid	negative	no	no			pulmonary congestion		42		14	0.6	132	3.9
3-Aug	352	152		5.2/2.8/2.4	hepatomegaly minimal free flid	negative	no	no			normal			20 days	76	1.6	158	6.5
2.8/1.2	112	46		2.8/1.2	hepatomegaly	negative	no	no			normal				52	0.5	130	2.6
1.9/1.2	657	413		3.5/1.8/1.7	hepatomegaly no free fluid	negative	no	no			normal			7 days	14	0.8	139	4.6
16.2/8.1	543	697		4.3/2.3/2.2	hepatomegaly free fluid	negative	no	no			bilateral pleral flid				209	3.6	138	4.1
<1	3249	2465		5.2/3.2/2	heoatomegaly increased echoes spleen normal no free fluid	negative	no	no			normal	lg	28		24	0.6	129	5.1
<1	233	433			hepatomegaly	negative	no	no			normal				28	0.5	133	4.3
2.2	233	122			hepatomegaly	negative	no	no			normal				32	0.8	134	4.2